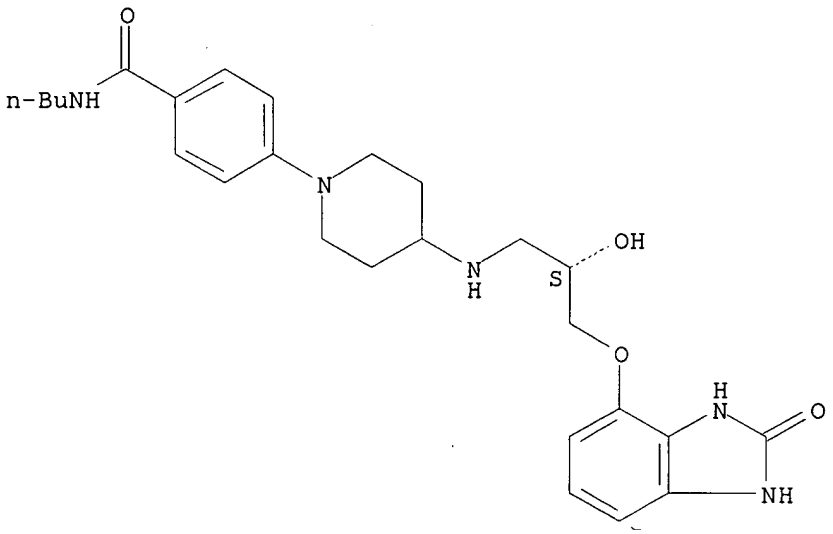
```
=> s l3
L4          35 L3

=> s l4 and benzimidaz?
        237882 BENZIMIDAZ?
L5           4 L4 AND BENZIMIDAZ?

=> d 1-4

L5   ANSWER 1 OF 4  REGISTRY  COPYRIGHT 2003 ACS on STN
RN   329280-03-7  REGISTRY
CN   Benzamide, N-butyl-4-[4-[[(2S)-3-[(2,3-dihydro-2-oxo-1H-benzimidazol-
     4-yl)oxy]-2-hydroxypropyl]amino]-1-piperidinyl]- (9CI)  (CA INDEX
     NAME)
FS   STEREOSEARCH
MF   C26 H35 N5 O4
SR   CA
LC   STN Files:   CA, CAPLUS

Absolute stereochemistry.
```

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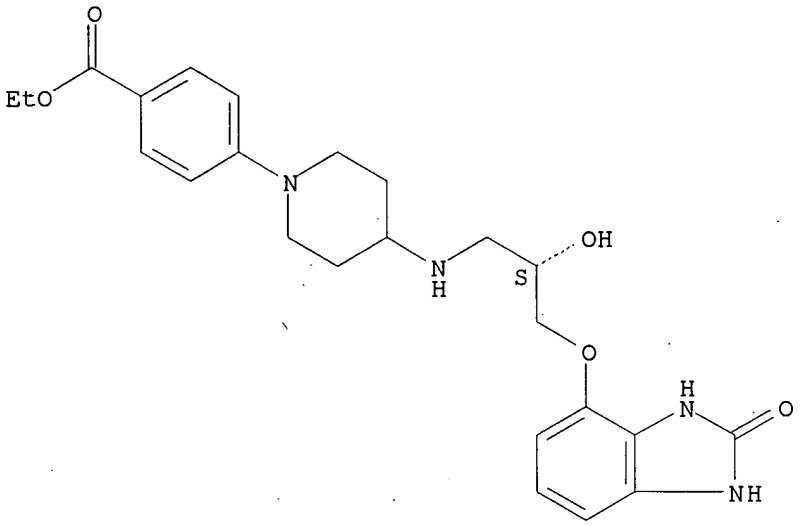
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

               1 REFERENCES IN FILE CA (1907 TO DATE)
               1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L5   ANSWER 2 OF 4  REGISTRY  COPYRIGHT 2003 ACS on STN
RN   329280-02-6  REGISTRY
CN   Benzoic acid, 4-[4-[[(2S)-3-[(2,3-dihydro-2-oxo-1H-benzimidazol-4-
     yl)oxy]-2-hydroxypropyl]amino]-1-piperidinyl]-, ethyl ester (9CI)
     (CA INDEX NAME)
OTHER NAMES:
CN   4-[4-[(2S)-2-Hydroxy-3-(2-oxo-2,3-dihydro-1H-benzimidazol-4-
     yloxy)propyl]amino]piperidin-1-yl]benzoic acid ethyl ester
FS   STEREOSEARCH
MF   C24 H30 N4 O5
SR   CA
LC   STN Files:   CA, CAPLUS, USPAT2, USPATFULL
```

Absolute stereochemistry.

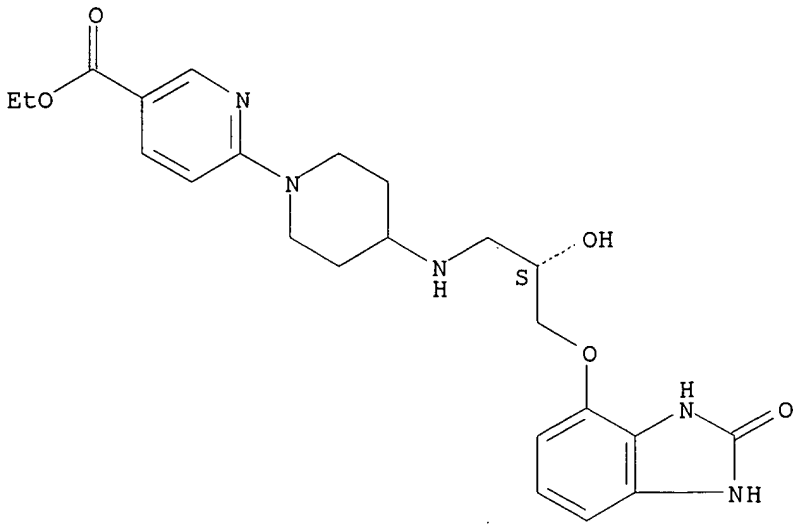


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L5 ANSWER 3 OF 4 REGISTRY COPYRIGHT 2003 ACS on STN
RN **329280-01-5** REGISTRY
CN **3-Pyridinecarboxylic acid, 6-[4-[[(2S)-3-[(2,3-dihydro-2-oxo-1H-benzimidazol-4-yl)oxy]-2-hydroxypropyl]amino]-1-piperidinyl]-, ethyl ester (9CI)** (CA INDEX NAME)
FS STEREOSEARCH
MF C23 H29 N5 O5
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

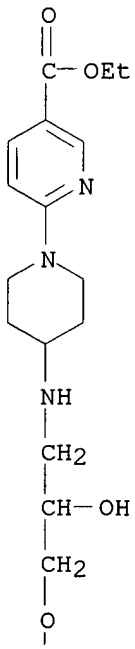


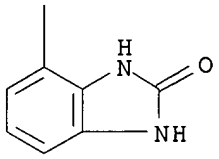
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L5 ANSWER 4 OF 4 REGISTRY COPYRIGHT 2003 ACS on STN
RN **329279-99-4** REGISTRY
CN **3-Pyridinecarboxylic acid, 6-[4-[[3-[(2,3-dihydro-2-oxo-1H-benzimidazol-4-yl)oxy]-2-hydroxypropyl]amino]-1-piperidinyl]-, ethyl ester (9CI)** (CA INDEX NAME)
FS 3D CONCORD
MF C23 H29 N5 O5
SR CA
LC STN Files: CA, CAPLUS

PAGE 1-A





PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> s l3 not l4

L7 0 L6 NOT L4

=> d shi
L7 HAS NO ANSWERS
L2 1 SEA FILE=CAPLUS WO200117989/PN
L3 ANALYZE L2 1 RN : 35 TERMS
L4 35 SEA FILE=REGISTRY L3
L6 35 SEA FILE=REGISTRY L3
L7 0 SEA FILE=REGISTRY L6 NOT L4

=> d his

(FILE 'HOME' ENTERED AT 12:36:24 ON 01 DEC 2003)

FILE 'CAPLUS' ENTERED AT 12:37:13 ON 01 DEC 2003
L1 0 S WO0117989/PN
L2 1 S WO200117989/PN
L3 ANALYZE L2 1 RN : 35 TERMS

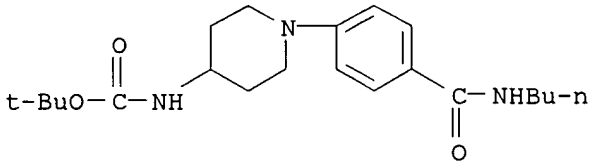
FILE 'REGISTRY' ENTERED AT 12:38:03 ON 01 DEC 2003
L4 35 S L3
L5 4 S L4 AND BENZIMIDAZ?
L6 35 S L3
L7 0 S L6 NOT L4

=> s l3 not l5

L9 31 L8 NOT L5

=> d scan

L9 31 ANSWERS REGISTRY COPYRIGHT 2003 ACS on STN
IN Carbamic acid, [1-[4-[(butylamino)carbonyl]phenyl]-4-piperidinyl]-, 1,1-dimethylethyl ester (9CI)
MF C21 H33 N3 O3

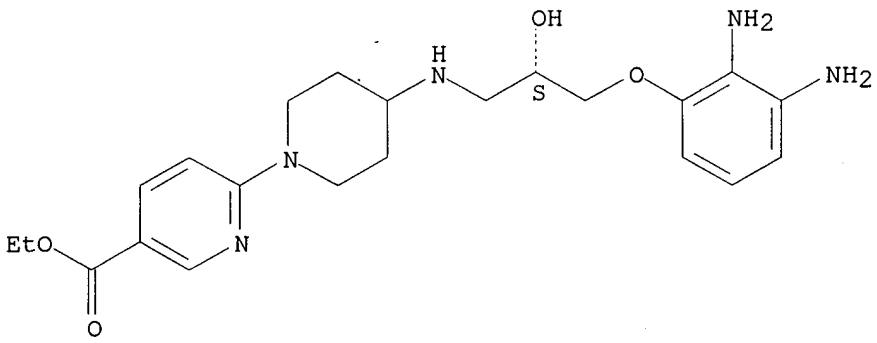


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):30

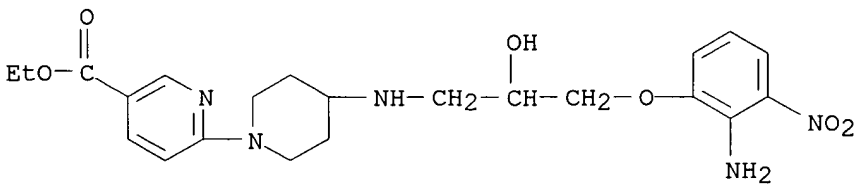
L9 31 ANSWERS REGISTRY COPYRIGHT 2003 ACS on STN
IN 3-Pyridinecarboxylic acid, 6-[4-[[(2S)-3-(2,3-diaminophenoxy)-2-hydroxypropyl]amino]-1-piperidinyl]-, ethyl ester (9CI)
MF C22 H31 N5 O4

Absolute stereochemistry.



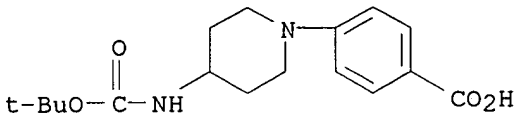
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L9 31 ANSWERS REGISTRY COPYRIGHT 2003 ACS on STN
IN 3-Pyridinecarboxylic acid, 6-[4-[[3-(2-amino-3-nitrophenoxy)-2-hydroxypropyl]amino]-1-piperidinyl]-, ethyl ester (9CI)
MF C22 H29 N5 O6



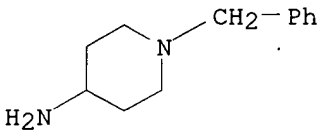
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L9 31 ANSWERS REGISTRY COPYRIGHT 2003 ACS on STN
IN Benzoic acid, 4-[4-[[(1,1-dimethylethoxy)carbonyl]amino]-1-piperidinyl]- (9CI)
MF C17 H24 N2 O4



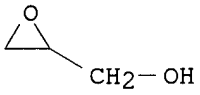
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L9 31 ANSWERS REGISTRY COPYRIGHT 2003 ACS on STN
IN 4-Piperidinamine, 1-(phenylmethyl)- (9CI)
MF C12 H18 N2
CI COM



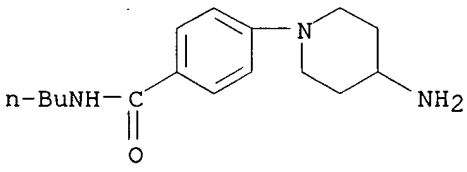
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L9 31 ANSWERS REGISTRY COPYRIGHT 2003 ACS on STN
IN Oxiranemethanol (9CI)
MF C3 H6 O2
CI COM



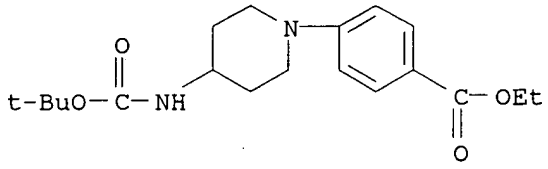
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L9 31 ANSWERS REGISTRY COPYRIGHT 2003 ACS on STN
IN Benzamide, 4-(4-amino-1-piperidinyl)-N-butyl-, monohydrochloride (9CI)
MF C16 H25 N3 O . Cl H



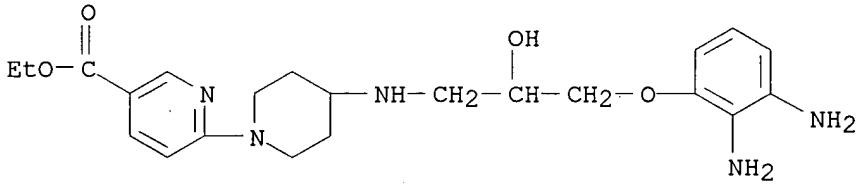
● HCl

L9 31 ANSWERS REGISTRY COPYRIGHT 2003 ACS on STN
IN Benzoic acid, 4-[4-[[(1,1-dimethylethoxy)carbonyl]amino]-1-piperidinyl]-, ethyl ester (9CI)
MF C19 H28 N2 O4



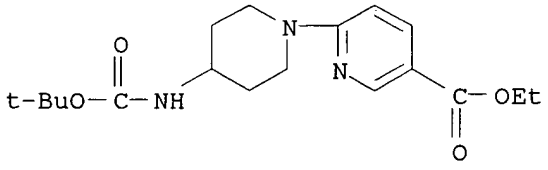
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L9 31 ANSWERS REGISTRY COPYRIGHT 2003 ACS on STN
IN 3-Pyridinecarboxylic acid, 6-[4-[[3-(2,3-diaminophenoxy)-2-hydroxypropyl]amino]-1-piperidinyl]-, ethyl ester (9CI)
MF C22 H31 N5 O4



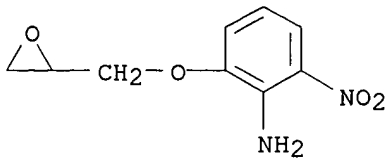
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L9 31 ANSWERS REGISTRY COPYRIGHT 2003 ACS on STN
IN 3-Pyridinecarboxylic acid, 6-[4-[[(1,1-dimethylethoxy)carbonyl]amino]-1-piperidinyl]-, ethyl ester (9CI)
MF C18 H27 N3 O4



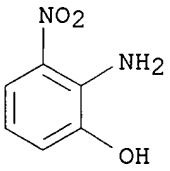
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L9 31 ANSWERS REGISTRY COPYRIGHT 2003 ACS on STN
IN Benzenamine, 2-nitro-6-(oxiranylmethoxy)- (9CI)
MF C9 H10 N2 O4



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

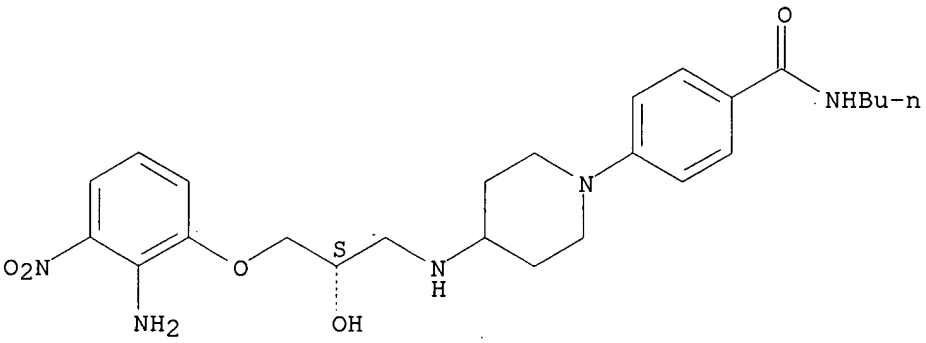
L9 31 ANSWERS REGISTRY COPYRIGHT 2003 ACS on STN
IN Phenol, 2-amino-3-nitro- (8CI, 9CI)
MF C6 H6 N2 O3
CI COM



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

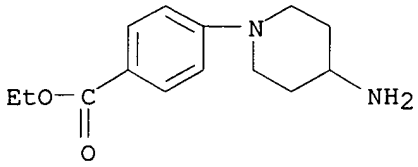
L9 31 ANSWERS REGISTRY COPYRIGHT 2003 ACS on STN
IN Benzamide, 4-[4-[[(2S)-3-(2-amino-3-nitrophenoxy)-2-hydroxypropyl]amino]-1-piperidinyl]-N-butyl- (9CI)
MF C25 H35 N5 O5

Absolute stereochemistry.



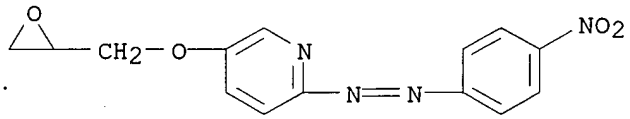
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L9 31 ANSWERS REGISTRY COPYRIGHT 2003 ACS on STN
IN Benzoic acid, 4-(4-amino-1-piperidinyl)-, ethyl ester, monohydrochloride (9CI)
MF C14 H20 N2 O2 . Cl H



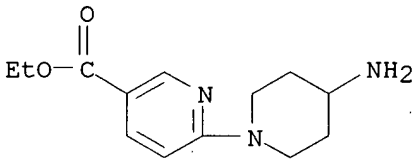
● HCl

L9 31 ANSWERS REGISTRY COPYRIGHT 2003 ACS on STN
IN Pyridine, 2-[(4-nitrophenyl)azo]-5-(oxiranylmethoxy)- (9CI)
MF C14 H12 N4 O4



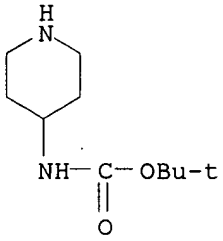
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L9 31 ANSWERS REGISTRY COPYRIGHT 2003 ACS on STN
IN 3-Pyridinecarboxylic acid, 6-(4-amino-1-piperidinyl)-, ethyl ester, dihydrochloride (9CI)
MF C13 H19 N3 O2 . 2 Cl H



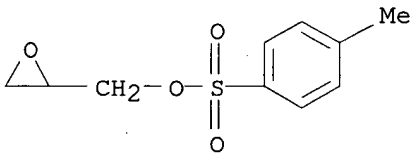
●2 HCl

L9 31 ANSWERS REGISTRY COPYRIGHT 2003 ACS on STN
IN Carbamic acid, 4-piperidinyl-, 1,1-dimethylethyl ester (9CI)
MF C10 H20 N2 O2
CI COM



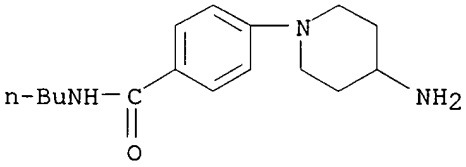
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L9 31 ANSWERS REGISTRY COPYRIGHT 2003 ACS on STN
IN Oxiranemethanol, 4-methylbenzenesulfonate (9CI)
MF C10 H12 O4 S
CI COM



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

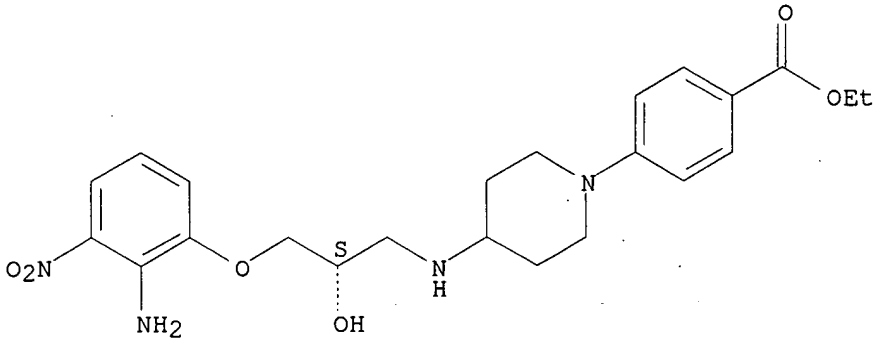
L9 31 ANSWERS REGISTRY COPYRIGHT 2003 ACS on STN
IN Benzamide, 4-(4-amino-1-piperidinyl)-N-butyl- (9CI)
MF C16 H25 N3 O
CI COM



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L9 31 ANSWERS REGISTRY COPYRIGHT 2003 ACS on STN
IN Benzoic acid, 4-[4-[[(2S)-3-(2-amino-3-nitrophenoxy)-2-hydroxypropyl]amino]-1-piperidinyl]-, ethyl ester (9CI)
MF C23 H30 N4 O6

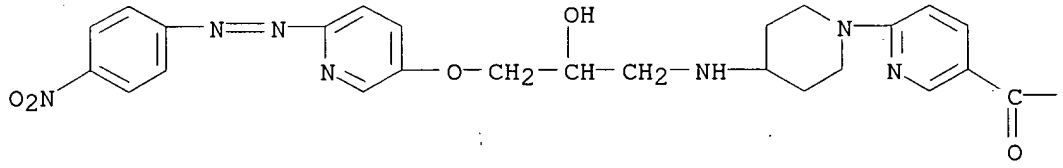
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L9 31 ANSWERS REGISTRY COPYRIGHT 2003 ACS on STN
IN 3-Pyridinecarboxylic acid, 6-[4-[[2-hydroxy-3-[[6-[(4-nitrophenyl)azo]-3-pyridinyl]oxy]propyl]amino]-1-piperidinyl]-, ethyl ester (9CI)
MF C27 H31 N7 O6

PAGE 1-A

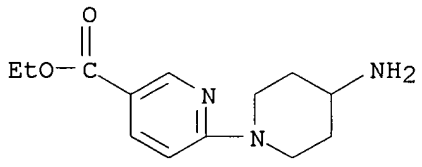


PAGE 1-B

—OEt

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

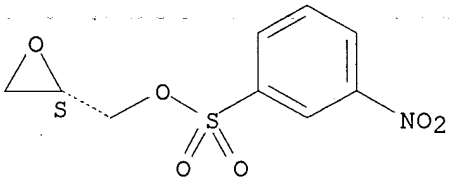
L9 31 ANSWERS REGISTRY COPYRIGHT 2003 ACS on STN
IN 3-Pyridinecarboxylic acid, 6-(4-amino-1-piperidinyl)-, ethyl ester (9CI)
MF C13 H19 N3 O2
CI COM



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

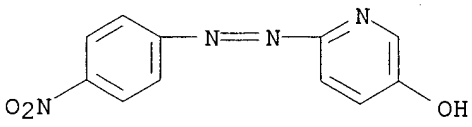
L9 31 ANSWERS REGISTRY COPYRIGHT 2003 ACS on STN
IN Benzenesulfonic acid, 3-nitro-, (2S)-oxiranylmethyl ester (9CI)
MF C9 H9 N O6 S

Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

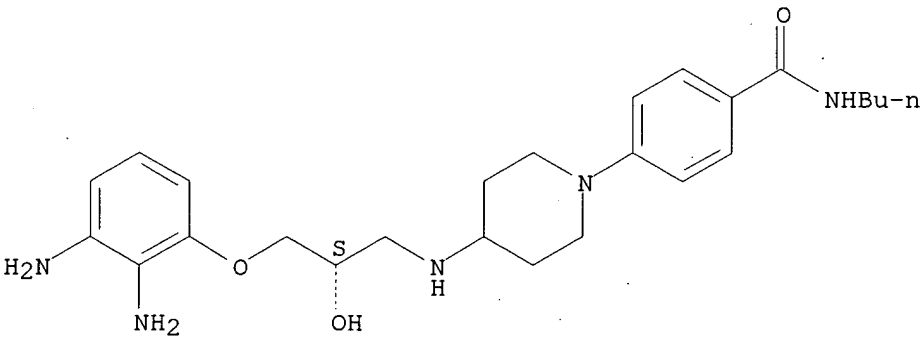
L9 31 ANSWERS REGISTRY COPYRIGHT 2003 ACS on STN
IN 3-Pyridinol, 6-[(4-nitrophenyl)azo]- (9CI)
MF C11 H8 N4 O3
CI COM



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L9 31 ANSWERS REGISTRY COPYRIGHT 2003 ACS on STN
IN Benzamide, N-butyl-4-[4-[[(2S)-3-(2,3-diaminophenoxy)-2-hydroxypropyl]amino]-1-piperidinyl]- (9CI)
MF C25 H37 N5 O3

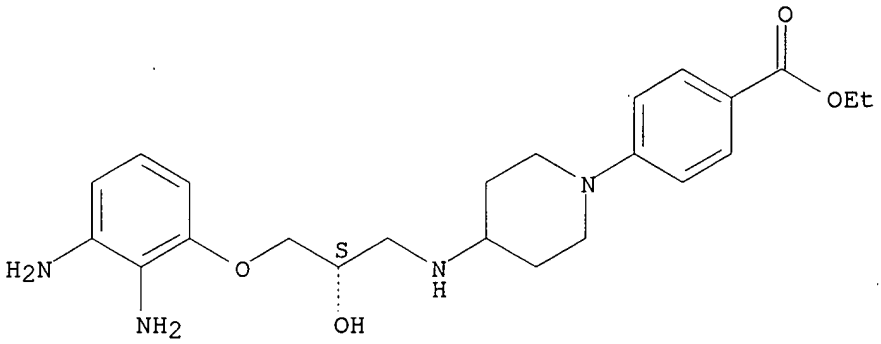
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L9 31 ANSWERS REGISTRY COPYRIGHT 2003 ACS on STN
IN Benzoic acid, 4-[4-[[(2S)-3-(2,3-diaminophenoxy)-2-hydroxypropyl]amino]-1-piperidinyl]-, ethyl ester (9CI)
MF C23 H32 N4 O4

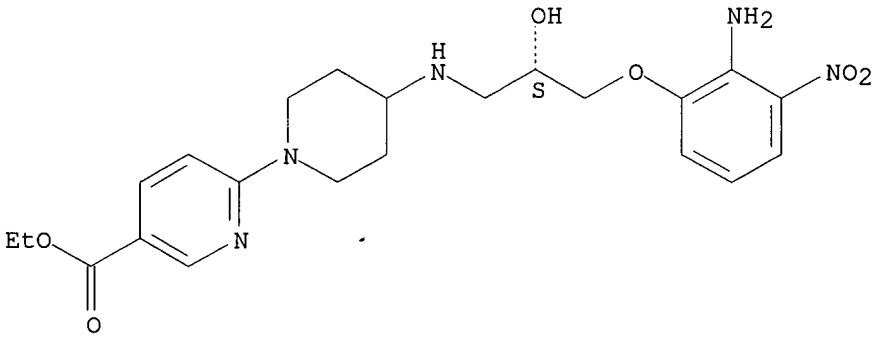
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

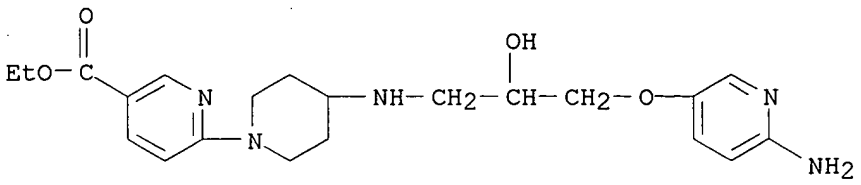
L9 31 ANSWERS REGISTRY COPYRIGHT 2003 ACS on STN
IN 3-Pyridinecarboxylic acid, 6-[4-[[(2S)-3-(2-amino-3-nitrophenoxy)-2-hydroxypropyl]amino]-1-piperidinyl]-, ethyl ester (9CI)
MF C22 H29 N5 O6

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

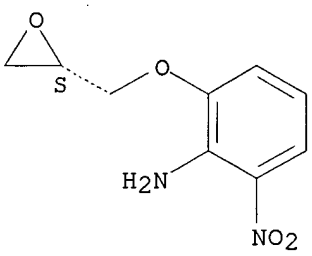
L9 31 ANSWERS REGISTRY COPYRIGHT 2003 ACS on STN
IN 3-Pyridinecarboxylic acid, 6-[4-[[3-[(6-amino-3-pyridinyl)oxy]-2-hydroxypropyl]amino]-1-piperidinyl]-, ethyl ester (9CI)
MF C21 H29 N5 O4



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

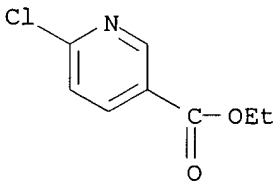
L9 31 ANSWERS REGISTRY COPYRIGHT 2003 ACS on STN
IN Benzenamine, 2-nitro-6-[(2S)-oxiranylmethoxy]- (9CI)
MF C9 H10 N2 O4

Absolute stereochemistry.



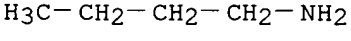
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L9 31 ANSWERS REGISTRY COPYRIGHT 2003 ACS on STN
IN 3-Pyridinecarboxylic acid, 6-chloro-, ethyl ester (9CI)
MF C8 H8 Cl N O2



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L9 31 ANSWERS REGISTRY COPYRIGHT 2003 ACS on STN
IN 1-Butanamine (9CI)
MF C4 H11 N
CI COM



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

ALL ANSWERS HAVE BEEN SCANNED

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L1                STR
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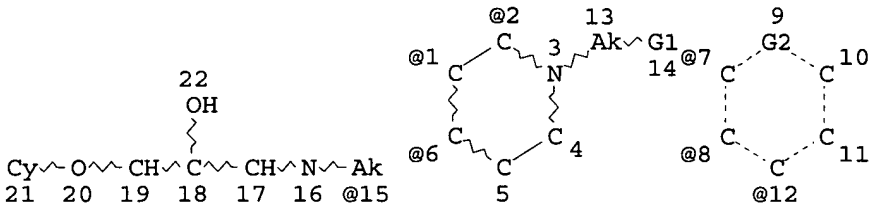


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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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NUMBER OF NODES IS  22

STEREO ATTRIBUTES: NONE


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FULL SCREEN SEARCH COMPLETED -  44645 TO ITERATE

100.0% PROCESSED   44645 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.02

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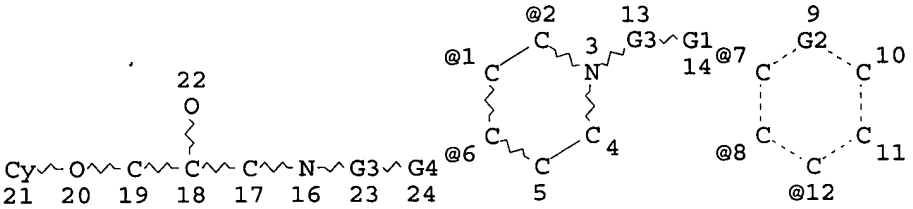
L5 STR



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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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NUMBER OF NODES IS 23

STEREO ATTRIBUTES: NONE

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SEARCH TIME: 00.00.07

L7 339 SEA SSS FUL L5

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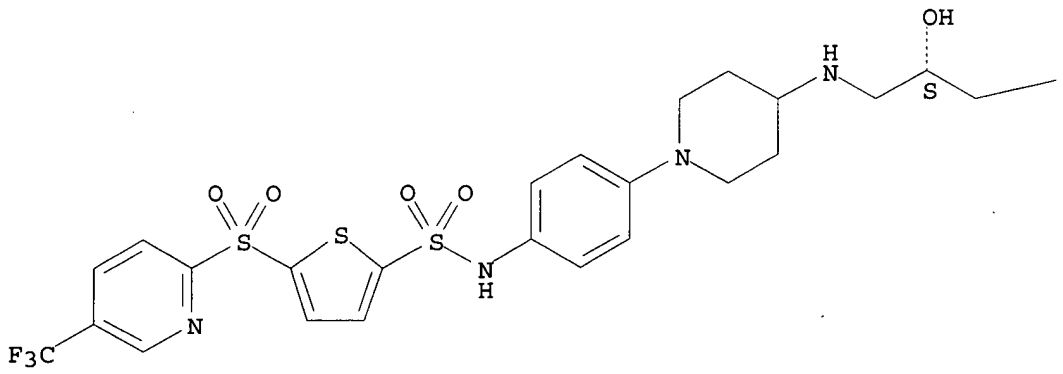
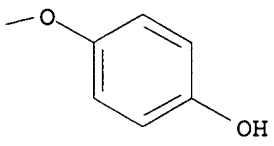
L7 339 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN 2-Thiophenesulfonamide, N-[4-[4-[[(2S)-2-hydroxy-3-(4-hydroxyphenoxy)propyl]amino]-1-piperidinyl]phenyl]-5-[[5-(trifluoromethyl)-2-pyridinyl]sulfonyl]- (9CI)
MF C30 H31 F3 N4 O7 S3

Absolute stereochemistry.

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L8                STR
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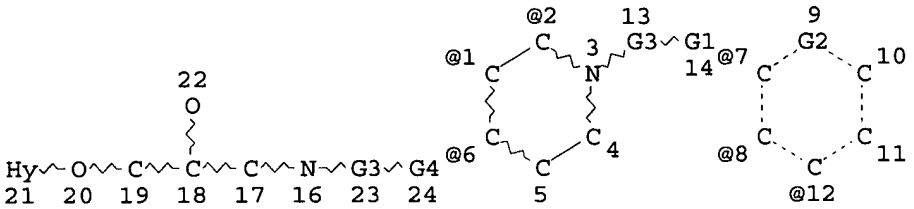


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VAR G2=C/N
REP G3=(0-2) CH
VAR G4=2/1/6
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC   8   6
NUMBER OF NODES IS  23

STEREO ATTRIBUTES: NONE


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ENTER SCOPE OF SEARCH (SAMPLE), FULL, RANGE, OR SUBSET:subset
ENTER SUBSET L# OR (END):l7
ENTER SUBSET SEARCH SCOPE - SAMPLE, FULL, RANGE, OR (END):ful
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FULL SUBSET SCREEN SEARCH COMPLETED -    339 TO ITERATE

100.0% PROCESSED     339 ITERATIONS                          109 ANSWERS
SEARCH TIME: 00.00.01

L9          109 SEA SUB=L7 SSS FUL L8

=> d scan

L9   109 ANSWERS   REGISTRY  COPYRIGHT 2003 ACS
IN   Benzenesulfonamide, N-[4-[4-[[(2S)-3-[(2,3-dihydro-2-oxo-1H-benzimidazol-4-
     yl)oxy]-2-hydroxypropyl]amino]-1-piperidinyl]phenyl]-2,5-dimethoxy- (9CI)
MF   C29 H35 N5 O7 S

Absolute stereochemistry.
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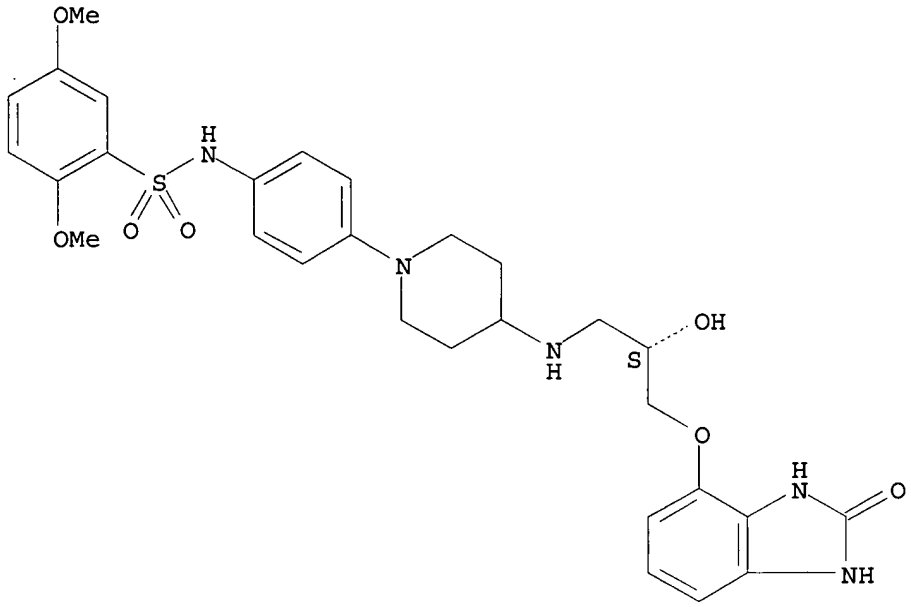
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NH

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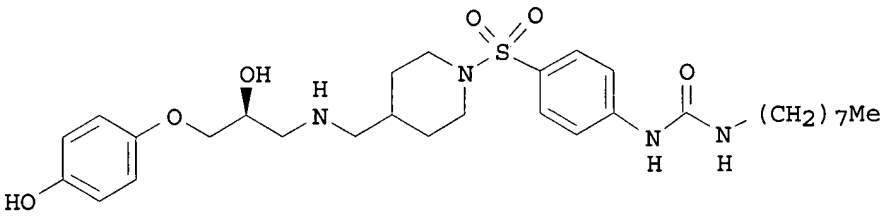
L10 19 L9

=> d bib abs 1-19

L10 ANSWER 1 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 2002:732389 CAPLUS
DN 138:237978
TI Novel substituted 4-aminomethylpiperidines as potent and selective human .beta.3-agonists. Part 1: Aryloxypropanolaminomethylpiperidines
AU Steffan, Robert J.; Ashwell, Mark A.; Solvibile, William R.; Matelan, Edward; Largis, Elwood; Han, Stella; Tillet, Jeffery; Mulvey, Ruth
CS Wyeth Research, Chemical Sciences, Collegeville, PA, 19426, USA
SO Bioorganic & Medicinal Chemistry Letters (2002), 12(20), 2957-2961
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
GI



I

AB The synthesis and SAR of a series of human .beta.3 adrenoreceptor agonists based on a template derived from a common pharmacophore coupled with 4-aminomethylpiperidine is described. Potent and selective agents were identified, such as I that was in vitro active in CHO cells expressing human .beta.3-AR (EC50=49 nM, IA = 1.1), and in vivo active in a transgenic mouse model.
RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

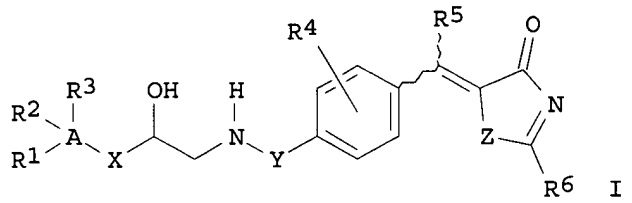
L10 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 2002:72096 CAPLUS
DN 136:134754
TI 2-Substituted thiazolidinones as beta-3 adrenergic receptor agonists, useful as antidiabetics and antiobesity agents
IN Hu, Baihua
PA American Home Products Corporation, USA
SO PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002006281	A1	20020124	WO 2001-US22526	20010716

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ,

VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6410734 B1 20020625 US 2001-904157 20010712
US 2002169325 A1 20021114 US 2002-132483 20020425
PRAI US 2000-218724P P 20000717
US 2001-904157 A3 20010712
OS MARPAT 136:134754
GI



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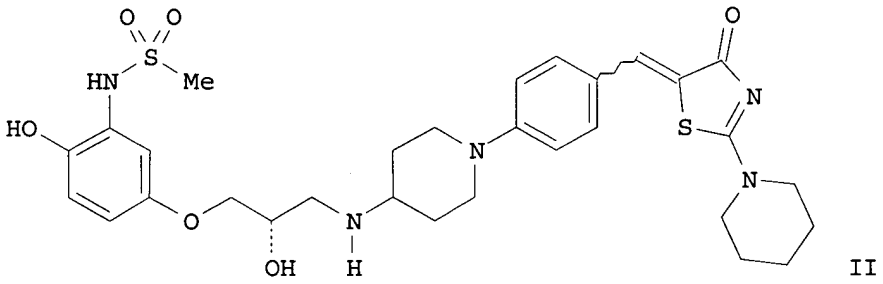

II

AB The invention provides compds. I or their pharmaceutically acceptable salts [A = aryl or selected heterocyclyl; X = OCH2, SCH2, or bond; Y = alkyl, alkoxy, azetidine, pyrrolidine, or piperidine (latter 3 attached to Ph via N atom); Z = S, O, NH, or N-alkyl; R1, R2, R3 = H, alkyl, cycloalkyl, OH, halo, CF3, alkoxy, PhCH2O, allyloxy, propargyloxy, acyloxy, cyano, NO2, (un)substituted amino, or 2 of these 3 substituents can combine to form an aryl-fused cycloalkyl optionally substituted by acylamino or OH; R4 = H, alkyl, alkoxy, OH, CO2H, or halo; R5 = H, alkyl; R6 = SCH3, (un)substituted NH2, amino acid or ester thereof (attached at amino), NHCONH2 or derivs., NHNHCONH2 or derivs.]. The compds. are selective .beta.3 adrenergic receptor agonists, useful in treating or inhibiting metabolic disorders related to insulin resistance or hyperglycemia (typically assocd. with obesity or glucose intolerance), atherosclerosis, gastrointestinal disorders, neurogenic inflammation, and frequent urination, and are particularly useful in the treatment or inhibition of type II diabetes. The compds. are also useful as feed additives, for increasing lean meat deposition and/or the ratio of lean meat to fat in animals, particularly mammals. Examples include 34 invention compd. syntheses and 38 intermediate prepns. For instance, N-benzyl-N-(2-benzyloxy-5-hydroxyphenyl)methanesulfonamide was etherified with (2S)-(+)-glycidyl 3-nitrobenzenesulfonate, and the resultant epoxide was aminated with dibenzylamine and hydrogenated to give N-[5-[((2S)-3-amino-2-hydroxypropyl)oxy]-2-hydroxyphenyl]methanesulfonamide. Reductive amination of a corresponding piperidinone deriv. by the latter compd. gave invention compd. II. This compd. bound to cloned human .beta.3 adrenoceptors in vitro with EC50 of 1 nM, and a maximal response comparable to isoproterenol.

RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 2002:72089 CAPLUS
DN 136:134678
TI Preparation of [(2-hydroxyethylamino)cyclylamino]arylsulfonamides as .beta.3 adrenergic receptor agonists
IN Sum, Fuk-Wah; Malamas, Michael Sotirios
PA American Home Products Corporation, USA
SO PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002006274	A1	20020124	WO 2001-US22379	20010716
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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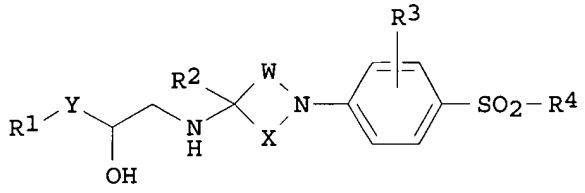
	US 2002028797	A1	20020307	US 2001-904114	20010712
	US 6444685	B2	20020903		
	US 2003027795	A1	20030206	US 2002-205019	20020725
PRAI	US 2000-218589P	P	20000717		
	US 2001-904114	A3	20010712		

OS MARPAT 136:134678
GI



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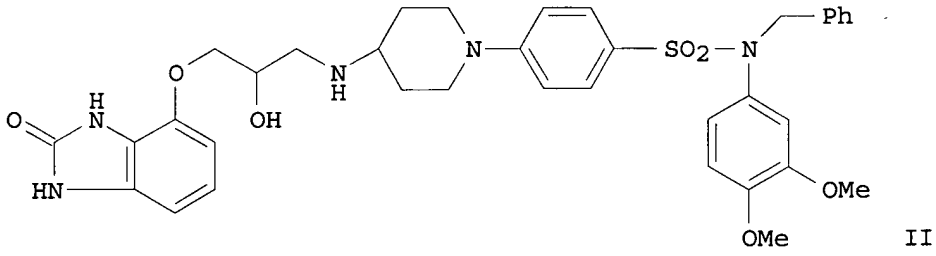

II

AB Title compds. I [wherein W = (CH2)m; X = (CH2)n; m = 1-3; n = 1-3; Y = OCH2, SCH2, or a bond; R1 = Ph, heterocyclyl, or heteroaryl substituted with R5 or R6; R2 = H, CF3, alkyl, alkenyl, or alkynyl; R4 = (cyclo)alkyl, alkenyl, alkynyl, OH, alkoxy, (hetero)aryloxy, (hetero)arylamino, alkoxycarbonylalkyl, carboxyalkyl, aminosulfonylalkyl, alkylsulfonylalkyl, or (un)substituted Ph, heterocyclyl, heteroaryl, acylamino, amino, etc.; R3, R5, and R6 = independently H, CF3, (cyclo)alkyl, alkenyl, alkynyl, aryl, heterocyclyl, heteroaryl, arylalkyl, halo, CN, NO2, OH, alkoxy, (hetero)aryloxy, alkylthio, arylthio, (hetero)arylamino,

alkylcarbonylalkyl, aminosulfonylalkyl, arylsulfonylalkyl, etc.; or a pharmaceutically acceptable salt thereof] were prepd. as .beta.3 adrenergic receptor agonists. For example, sodium triacetoxyborohydride was added to a soln. of 4-[(2S)-3-amino-2-hydroxypropoxy]-1,3-dihydrobenzimidazol-2-one, N-benzyl-N-(3,4-dimethoxyphenyl)-4-(4-oxopiperidin-1-yl)sulfonamide, and AcOH in anhyd. DMF. The reaction was stirred overnight and then quenched with 50% H2O/satd. NaHCO3 to give II. The latter exhibited selective binding to the .beta.3 adrenergic receptor (EC50 0.017 .mu.M) compared to the .beta.1 and .beta.2 adrenergic receptors. Thus, I are useful in treating metabolic disorders related to insulin resistance or hyperglycemia (typically assocd. with obesity or glucose intolerance), atherosclerosis, gastrointestinal disorders, neurogenetic inflammation, glaucoma, ocular hypertension, and frequent urination, and are particularly useful in the treatment of type II diabetes.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 2002:72070 CAPLUS
DN 136:134677
TI Substituted 2-(S)-hydroxy-3-[(piperidin-4-yl-methyl)amino]propyl ethers and substituted 2-aryl-2-(R)-hydroxy-1-(piperidin-4-yl-methyl)ethylamines as beta-3 adrenergic receptor agonists, antidiabetics, and antiobesity agents
IN Steffan, Robert John; Ashwell, Mark Anthony; Pelletier, Jeffrey Claude; Solvibile, William Ronald; Matelan, Edward Martin
PA American Home Products Corporation, USA
SO PCT Int. Appl., 216 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002006255	A2	20020124	WO 2001-US22363	20010716
	WO 2002006255	A3	20020321		
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2002037907	A1	20020328	US 2001-903738	20010712
	US 6506901	B2	20030114		
PRAI	US 2000-218753P	P	20000717		

OS MARPAT 136:134677
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention provides title compds. I and their pharmaceutically acceptable salts [wherein A = OCH2, bond; R = (un)substituted aryl or certain N/O/S heterocyclyl; R1 = (cyclo)alkyl, alkoxy, (cyclo)alkylamino, (un)substituted aryl, arylamino, arylalkyl, or heterocyclyl; Z = bond, SO2, CO]. I are useful in treating or inhibiting metabolic disorders related to insulin resistance or hyperglycemia (typically assocd. with

obesity or glucose intolerance), atherosclerosis, gastrointestinal disorders, neurogenic inflammation, glaucoma, ocular hypertension, and frequent urination. The compds. are particularly useful in the treatment or inhibition of type II diabetes. They are also useful for increasing lean meat deposition and/or increasing the lean meat to fat ratio in animals, particularly mammals. Approx. 240 individual compds. and addnl. salts were prepd. by either std. or combinatorial methods. For instance, invention compd. II was prepd. by reaction of the (S)-isomeric epoxide III with the corresponding amine. II had an EC50 of 0.001 .mu.M against cloned human .beta.3 adrenoceptors in vitro, with a maximal response comparable to isoproterenol.

L10 ANSWER 5 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 2002:72047 CAPLUS
DN 136:134676
TI Preparation of cyclic amine phenyl .beta.3 adrenergic receptor agonists for treatment of metabolic disorders related to insulin resistance or hyperglycemia
IN Hu, Baihua; Sum, Fuk-Wah; Malamas, Michael Sotirios
PA American Home Products Corporation, USA
SO PCT Int. Appl., 235 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002006232	A1	20020124	WO 2001-US22387	20010716
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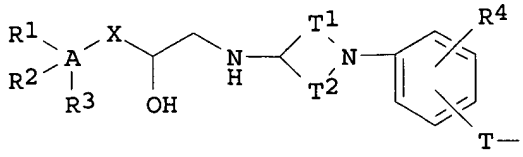
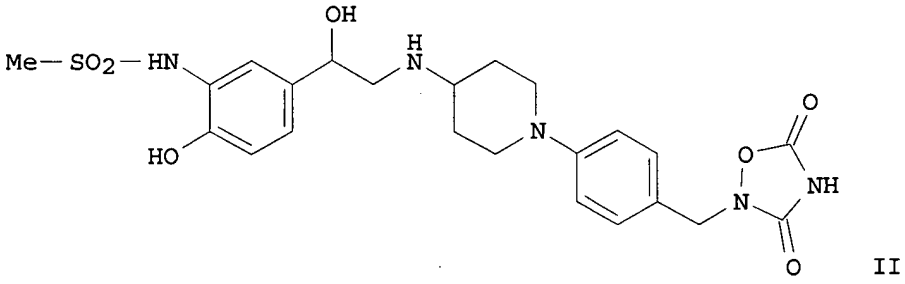
	US 2002028835	A1	20020307	US 2001-903754	20010712
	US 6525202	B2	20030225		
	EP 1301482	A1	20030416	EP 2001-984234	20010716
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRAI	US 2000-218627P	P	20000717		
	WO 2001-US22387	W	20010716		

OS MARPAT 136:134676
GI



I



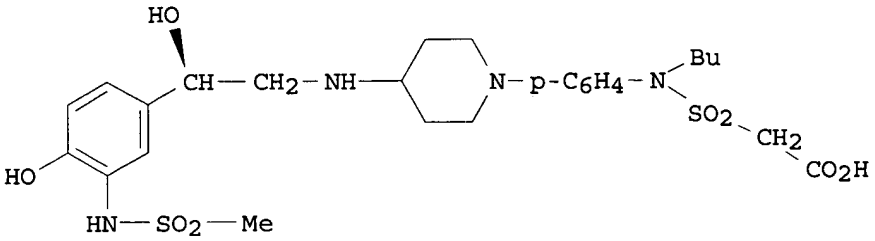
II

AB Title compds. I [wherein A = (hetero)aryl or heterocyclyl; X = OCH2, SCH2, or a bond; T1 = (CH2)m; T2 = (CH2)n; m = 1-3; n = 1-3; T = a bond, (un)substituted alkyl or alkenyl, alkynyl, alkylthio, alkylamino, alkoxy(alkyl), alkylthioalkyl, acyl, or alkenylcarbonyl; R1, R2, and R3 = independently H, (cyclo)alkyl, OH, halo, CF3, alkoxy, benzyloxy, allyloxy, propargyloxy, acyloxy, CN, NO2, NH2, CONH2, (di)alkylamino, formamido, ureido, acylamino, alkylsulfonylamino, arylsulfonylamino, dialkyloxyphosphorylamino, dihydroxyphosphorylamino, alkoxycarbonyl, or (un)substituted aryl; R4 = H, alkyl, halo, OH, alkoxy, alkylthio, (alkyl)amino, carboxy, acyl, arylcarbonyl, alkoxycarbonyl, CONH2, alkylaminocarbonyl, alkylsulfonyl, or arylsulfonylamino; R5 = (un)substituted (di)oxoimidazolidinyl, (di)oxooxazolidinyl, (di)oxothiazolidinyl, dioxooxadiazolidinyl, tetrazolyl, oxopyrrolinyl, alkoxycarbonyl, aminocarbonyl, acyl, ureido, etc.; or a pharmaceutically acceptable salt thereof] were prepd. by std. and combinatorial synthetic methods as .beta.3 adrenergic receptor agonists. For example, acetic acid was added to a mixt. of N-[5-[(1R)-2-amino-1-hydroxyethyl]-2-hydroxyphenyl]methanesulfonamide (prepn. given), 2-[4-(4-oxo-1-piperidinyl)benzyl]-1,2,4-oxadiazolidine-3,5-dione, and DMF. Sodium triacetoxyborohydride was added and the mixt. stirred at room temp. for 24 h to give (R)-I (71%). The latter bound to the .beta.3 adrenergic receptor with EC50 of 20 .mu.M, exhibited a maximal response activity equiv. to isoproterenol, and increased thermogenesis in .beta.3 transgenic mice by 30 .+-. 8% compared to an increase of 16 .+-. 4% in .beta.3 knockout mice. Thus, I are useful in treating or inhibiting metabolic disorders related to insulin resistance or hyperglycemia (typically assocd. with obesity or glucose intolerance), atherosclerosis, gastrointestinal disorders, neurogenetic inflammation, glaucoma, ocular hypertension, frequent urination, and are particularly useful in the treatment or inhibition II diabetes.

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 6 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 2001:591187 CAPLUS
DN 135:352336
TI Novel (4-Piperidin-1-yl)-phenyl Sulfonamides as Potent and Selective Human .beta.3 Agonists
AU Hu, B.; Ellingboe, J.; Han, S.; Largis, E.; Lim, K.; Malamas, M.; Mulvey, R.; Niu, C.; Oliphant, A.; Pelletier, J.; Singanallore, T.; Sum, F.-W.; Tillett, J.; Wong, V.
CS Wyeth-Ayerst Research, Chemical Sciences, Pearl River, NY, 10965, USA
SO Bioorganic & Medicinal Chemistry (2001), 9(8), 2045-2059

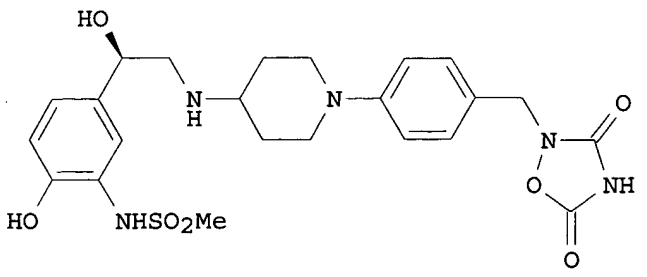
CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier Science Ltd.
DT Journal
LA English
GI



I

AB A series of novel (4-piperidin-1-yl)-Ph sulfonamides was prepd. and evaluated for their biol. activity on the human .beta.3-adrenergic receptor (AR). Replacement of the 3,4-dihydroxyl group of the catechol moiety with 4-hydroxyl-3-Me sulfonamide on the left-hand side of the compds. resulted in a no. of potent full agonists at the .beta.3 receptor. Modification of the right-hand side of the compds. by incorporation of a free carboxylic acid resulted in a few potent human .beta.3 agonists with low affinities for .beta.1- and .beta.2-ARs. N-Alkyl substitution on the 4-piperidin-1-yl-phenylamine further increased the .beta.3 potency while maintaining the selectivity. For example, sulfonamide I is a potent full .beta.3 agonist (EC50=0.004 .mu.M, IA=1.0) with >500-fold selectivity over .beta.1- and .beta.2-ARs.
RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 2001:279027 CAPLUS
DN 135:107284
TI New oxadiazolidinedione derivatives as potent and selective human .beta.3 agonists
AU Hu, B.; Malamas, M.; Ellingboe, J.; Largis, E.; Han, S.; Mulvey, R.; Tillett, J.
CS Chemical Sciences, Wyeth-Ayerst Research, Pearl River, NY, 10965, USA
SO Bioorganic & Medicinal Chemistry Letters (2001), 11(8), 981-984
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
GI



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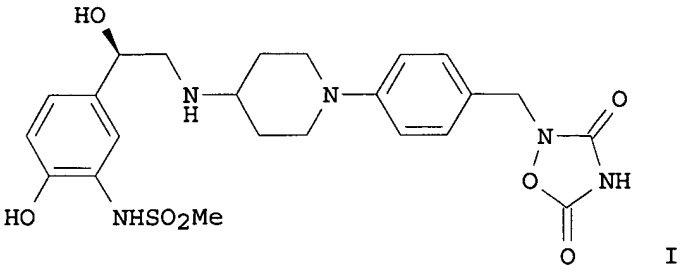


I

AB A series of thiazolidinediones and oxadiazolidinediones was prepd. and evaluated for their biol. activity on the human .beta.3-adrenergic receptor. The oxadiazolidinedione I was found to be the most potent and selective compd. in this study, with an EC50 value of 0.02 .mu.M at the .beta.3 receptor, 259-fold selectivity over the .beta.1 receptor, and 745-fold selectivity over the .beta.2 receptor.

RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 8 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 2001:207056 CAPLUS
DN 135:40409
TI 2,4-thiazolidinediones as potent and selective human .beta.3 agonists
AU Hu, B.; Ellingboe, J.; Gunawan, I.; Han, S.; Largis, E.; Li, Z.; Malamas, M.; Mulvey, R.; Oliphant, A.; Sum, F.-W.; Tillett, J.; Wong, V. W.
CS Chemical Sciences, Wyeth-Ayerst Research, Pearl River, NY, 10965, USA
SO Bioorganic & Medicinal Chemistry Letters (2001), 11(6), 757-760
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
AB Methylsulfonamide substituted 2,4-thiazolidinedione is a potent (EC50=0.01 .mu.M, IA=1.19) and selective (more than 110-fold over .beta.1 and .beta.2 agonist activity) .beta.3 agonist. This compd. has also been proven to be active and selective in an in vivo mode.

RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 9 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 2001:185745 CAPLUS
DN 134:222636
TI Preparation of heteroaryloxy propanolamines and pharmaceutical compositions containing same
IN Cecchi, Roberto; Oliva, Ambrogio
PA Sanofi-Synthelabo, Fr.
SO PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001017989	A2	20010315	WO 2000-FR2482	20000908
WO 2001017989	A3	20010614		

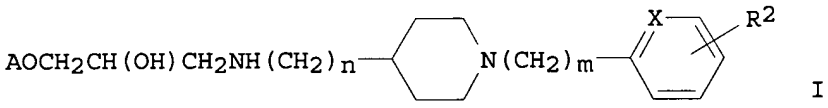
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

	FR 2798126	A1	20010309	FR 1999-11204	19990908
	FR 2798126	B1	20011019		
	EP 1214313	A2	20020619	EP 2000-962583	20000908
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
	JP 2003508528	T2	20030304	JP 2001-522212	20000908
PRAI	FR 1999-11204	A	19990908		
	WO 2000-FR2482	W	20000908		

OS MARPAT 134:222636

GI



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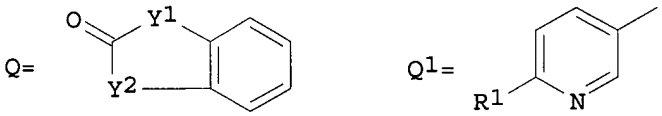


AB The title compds. I [X = N, CH; A = Q, Q1; R1 = H, NH2, NR3R4, NR3CO(C1-C4)Alk, NR3SO2(C1-C4)Alk; R2 = H, halo, (C1-C4)Alk, (C1-C4)alkoxyl, COOH, COO(C1-C4)Alk, cyano, CONR3R4, NO2, SO2NR3R4, NHSO2(C1-C4)Alk group; m and n represent 0, 1 or 2; R3, R4 = H, (C1-C4)Alk group; Y1, Y2 = NH, O] were prepd. E.g., a multistep synthesis of 3-[1-(5-ethoxycarbonylpyrid-2-yl)-4-piperidinylamino]-1-[1,2-dihydro-2-oxo-benzimidazol-4-yloxy]-2-propanol is described.

L10 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2003 ACS

AN 2000:842112 CAPLUS

DN 134:17502

TI Preparation of phenoxypropylamine compounds as antagonists of 5-HT1A receptor

IN Nishiyama, Akira; Bougauchi, Masahiro; Kuroita, Takanobu; Minoguchi, Masanori; Morio, Yasunori; Kanzaki, Kouji

PA Welfide Corp., Japan

SO PCT Int. Appl., 335 pp.
CODEN: PIXXD2

DT Patent

LA Japanese

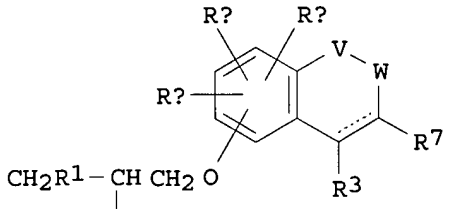
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000071517	A1	20001130	WO 2000-JP3279	20000522
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	BR 2000011542	A	20020305	BR 2000-11542	20000522
	EP 1188747	A1	20020320	EP 2000-927844	20000522
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

	US 2002111358	A1	20020815	US 2001-990389	20011123
PRAI	JP 1999-142750	A	19990524		
	JP 1999-166160	A	19990614		
	JP 1999-277384	A	19990929		
	JP 2000-18080	A	20000125		
	WO 2000-JP3279	W	20000522		

OS MARPAT 134:17502

GI



I

AB Phenoxypropylamine compds. represented by general formula [I; a bond represented by a solid and a dotted line is a double or single bond; X = H, HO, C1-8 alkoxy, acyloxy, oxo; R1 = 4-substituted piperidino, piperazino, 1-piperidinylamino, or 1,2,3,6-tetrahydropyrazinyl, (un)substituted aryloxy- or arylthioamino, (un)substituted heterocyclyloxy- or heterocyclylthioamino, etc.; R3 = H, C1-18 alkyl, halo; Ra, Rb, Rc = H, C1-18 alkyl, OH, C1-8 alkoxy, halo, acyl, NO2, NH2], optically active isomers thereof or pharmaceutically acceptable salts thereof and hydrates of the same are prepd. These compds. have an affinity selectively for 5-HT1A receptor, simultaneously show an antagonistic activity, and inhibit the reuptake of 5-HT, thereby being usable as antidepressant agents quickly achieving an antidepressant effect (no data). Thus, 4-(3,4-dichlorophenyl)piperazine was added to a soln. of (S)-5-(4-glycidyloxybenzo[b]furan-2-yl)-3-methylisoxazole in MeOH and refluxed for 8 h to give (S)-1-(4-(3,4-dichlorophenyl)piperazin-1-yl)-3-(2-(3-methylisoxazol-5-yl)benzo[b]furan-4-yloxy)-2-propanol.

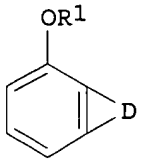
RE.CNT 151 THERE ARE 151 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 1998:545375 CAPLUS
DN 129:148993
TI Preparation and formulation of .omega.-(heteroaryloxy)alkanamines as serotonin reuptake inhibitors and 5-HT1A receptor ligands
IN Audia, James E.; Hibschman, David J.; Krushinski, Joseph H., Jr.; Mabry, Thomas E.; Nissen, Jeffrey S.; Rasmussen, Kurt; Rocco, Vincent P.; Schaus, John M.; Thompson, Dennis C.; Wong, David T.
PA Eli Lilly Co., USA
SO U.S., 67 pp., Cont.-in-part of U. S. Ser. No. 373,823, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5789402	A	19980804	US 1995-471121	19950606
	CN 1178530	A	19980408	CN 1996-192598	19960111
PRAI	US 1995-373823	B2	19950117		

OS MARPAT 129:148993

GI



I

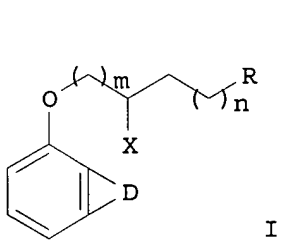
AB Title compds. [I; R1 = (CH2)rCHXCH2(CH2)sR; r = 0-4; s = 0-1; D = a residue which combines with the carbon atoms to which it is attached to complete a pyrrolyl group; X = H, Ph, OH, MeO; R = (un)substituted piperazino, piperidino, etc.] were prepd as serotonin reuptake inhibitors and 5-HT1A receptor ligands (no data). Thus, refluxing of (S)-(+)-4-(oxiranylmethoxy)-1H-indole with 4-amino-1-benzylpiperidine in MeOH gave (2S)-(-)-I [R1 = CH2CH(OH)CH2R, R = 1-benzyl-4-piperidinylamino].

RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 1998:250697 CAPLUS
DN 128:294709
TI Heterocyclyloxyalkanamines having effects on serotonin-related systems
IN Hibschman, David J.; Krushinski, Joseph H., Jr.; Rasmussen, Kurt; Rocco, Vincent P.; Schaus, John M.; Thompson, Dennis C.
PA Eli Lilly and Co., USA
SO U.S., 65 pp., Cont.-in-part of U.S. Ser. No. 373,823, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5741789	A	19980421	US 1995-467434	19950606
	CN 1178530	A	19980408	CN 1996-192598	19960111
	US 6172073	B1	20010109	US 1998-49837	19980327
PRAI	US 1995-373823	B2	19950117		
	US 1995-467434	A3	19950606		

OS MARPAT 128:294709
GI



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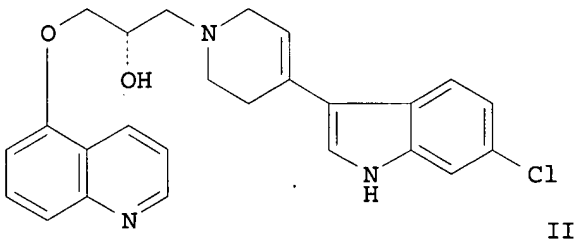


II

AB A series of heterocyclyloxy-substituted alkanamines I [m = 0-4; n = 0-1; D = atoms to complete fused pyrrolo, imidazolo, pyrido, pyrazino, pyridazino, or pyrimido nucleus (only pyrido is claimed); X = H, Ph, OH, OMe; X = H or Ph when m = 0; R = certain (un)substituted cyclic, bicyclic, and spirocyclic amino groups] are effective pharmaceuticals for the treatment of conditions related to or affected by the reuptake of serotonin and by the serotonin 1A receptor (no data). Some I show a unique combination of 5-HT1A receptor activity and serotonin reuptake

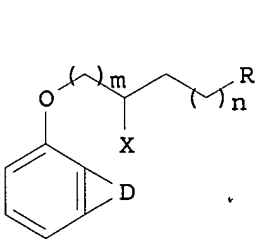
inhibition. I are particularly useful for alleviating the symptoms of nicotine and tobacco withdrawal, and for the treatment of depression and other conditions for which serotonin reuptake inhibitors are used. Over 200 synthetic examples and 7 std. formulation examples are given. In the only example of a claimed compd. (quinoline-derived, D = pyrido), reaction of (R)-5-(oxiranylmethoxy)quinoline with 6-chloro-2-(1,2,3,6-tetrahydropyridin-4-yl)-1H-indole in EtOH gave the preferred compd. II in 87% yield.

RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 1997:344806 CAPLUS
DN 127:34133
TI Heterocyclyloxyalkanamines having effects on serotonin-related systems
IN Audia, James E.; Hibschman, David J.; Krushinski, Joseph H., Jr.; Mabry, Thomas E.; Nissen, Jeffrey S.; Rasmussen, Kurt; Rocco, Vincent P.; Schaus, John M.; Thompson, Dennis C.; Wong, David T.
PA Eli Lilly and Company, USA
SO U.S., 65 pp., Cont.-in-part of U.S. Ser. No. 373,823, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5627196	A	19970506	US 1995-468948	19950606
	CN 1178530	A	19980408	CN 1996-192598	19960111
PRAI	US 1995-373823	B2	19950117		

OS MARPAT 127:34133
GI



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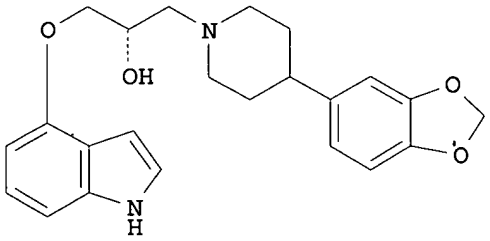


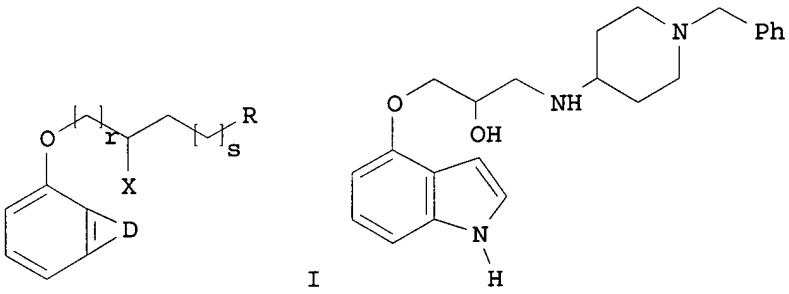
II

AB A series of heterocyclyloxy-substituted alkanamines I [m = 0-4; n = 0-1; D = atoms to complete fused pyrrolo, imidazolo, pyrido, pyrazino, pyridazino, or pyrimido nucleus; X = H, Ph, OH, OMe; X = H or Ph when r = 0; R = (un)substituted piperidino, piperazino, piperidinylamino, piperazinoamino, morpholinoamino, certain spirocyclic amino substituents, etc.] are effective pharmaceuticals for the treatment of conditions related to or affected by the reuptake of serotonin and by the serotonin 1A receptor (no data). Some I show a unique combination of 5-HT1A receptor activity and serotonin reuptake inhibition. I are particularly useful for alleviating the symptoms of nicotine and tobacco withdrawal, and for the treatment of depression and other conditions for which serotonin reuptake inhibitors are used. Over 200 synthetic examples and 7 std. formulation examples are given. For instance, reaction of (S)-(+)-4-(oxiranylmethoxy)-1H-indole with 4-(3,4-methylenedioxyphenyl)piperidine gave a preferred title compd., II, isolated as the oxalate in 71% overall yield.

L10 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 1997:260110 CAPLUS
DN 126:305591
TI Preparation of heteroaryloxy alkanamines having effects on serotonin-related systems
IN Audia, James E.; Krushinski, Joseph H., Jr.; Rasmussen, Kurt; Rocco, Vincent P.; Schaus, John M.; Thompson, Dennis C.; Wong, David T.
PA Eli Lilly and Company, USA
SO U.S., 63 pp., Cont.-in-part of U.S. Ser. No. 373,823, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5614523	A	19970325	US 1995-470512	19950606
	CN 1178530	A	19980408	CN 1996-192598	19960111
PRAI	US 1995-373823	B2	19950117		

OS MARPAT 126:305591
GI



I II

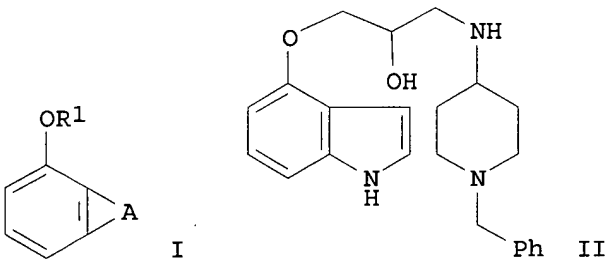
AB The title compds. [I; r = 0-4; s = 0-1; D = a residue which combines with the carbon atoms to which it is attached to complete a pyrrolyl group; X = H, Ph, OH, MeO; R = (un)substituted piperazino, piperidino, etc.], useful for the treatment of conditions related to or affected by the reuptake of serotonin and by the serotonin 1A receptor, were prepd. and formulated. Thus, refluxing of (S)-(+)-4-(oxiranylmethoxy)-1H-indole with 4-amino-1-benzylpiperidine in MeOH afforded 78% (2S)-(-)-II. Compds. I are effective at 20-25 mg/day when administered to a patient in need of or carrying out a redn. or cessation of tobacco or nicotine use. Compds. I are particularly useful for alleviating the symptoms of nicotine and tobacco withdrawal, and for the treatment of depression, anxiety, hypertension, cognitive disorders, psychosis, sleep disorders, gastric motility disorders, sexual dysfunction, brain trauma, memory loss, eating disorders and obesity, substance abuse, obsessive-compulsive disorder, panic disorder, migraine, pain, bulimia, premenstrual syndrome, late luteal syndrome, alcoholism, dementia of aging, social phobia, attention deficit hyperactivity disorder, impulsive control disorders, chronic fatigue syndrome, premature ejaculation, anorexia nervosa, and autism.

L10 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 1997:15489 CAPLUS
DN 126:74755
TI Preparation and formulation of 4-(3-amino-2-hydroxypropoxy)indoles and analogs as 5-HT1A receptor ligands
IN Krushinski, Joseph H., Jr.; Rasmussen, Kurt; Rocco, Vincent P.; Schaus, John M.; Thompson, Dennis C.
PA Eli Lilly and Company, USA

SO U.S., 63 pp., Cont.-in-part of U.S. Ser. No. 383,823,abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 6

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5576321	A	19961119	US 1995-468900	19950606
CA 2210220	AA	19960725	CA 1996-2210220	19960111
WO 9622290	A1	19960725	WO 1996-US41	19960111
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, US				
RW: KE, LS, MW, SD, SZ, UG, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9646516	A1	19960807	AU 1996-46516	19960111
AU 718875	B2	20000420		
BR 9607077	A	19971118	BR 1996-7077	19960111
CN 1178530	A	19980408	CN 1996-192598	19960111
JP 10512861	T2	19981208	JP 1996-522282	19960111
EP 722941	A2	19960724	EP 1996-300286	19960115
EP 722941	A3	20000412		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
NO 9703281	A	19970908	NO 1997-3281	19970715
FI 9703024	A	19970716	FI 1997-3024	19970716
PRAI US 1995-373823	B2	19950117		
US 1995-468900	A	19950606		
WO 1996-US41	W	19960111		

OS MARPAT 126:74755
GI



I II

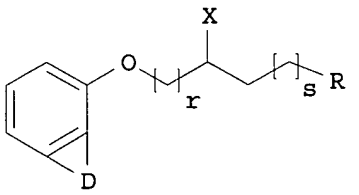
AB Title compds. [I; A = atoms to complete an N-contg. heterocyclic ring; R1 = (CH2)rCHR2CH2(CH2)sR; R = alkylamino, azinylamino, N-attached heterocyclyl, etc.; R2 = H, OH, OMe, Ph; r = 0-4; s = 0-1] were prepd. as 5-HT1A receptor ligands (no data). Thus, (S)-4-oxiranylmethoxy-1H-indole was aminated by 4-amino-1-benzylpiperidine to give title compd. (S)-II.

L10 ANSWER 16 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 1996:509758 CAPLUS
DN 125:168021
TI Preparation of 3-(4-indolyloxy)-2-hydroxypropanamines as serotonin 1A receptor antagonists and partial agonists
IN Audia, James E.; Hibschman, David J.; Krushinski, Jr Joseph H.; Mabry, Thomas E.; Nissen, Jeffrey S.; Rasmussen, Kurt; Rocco, Vincent P.; Schaus, John M.; Thompson, Dennis C.; Wong, David T.
PA Lilly, Eli, and Co., USA
SO Eur. Pat. Appl., 112 pp.

CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 6

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 722941	A2	19960724	EP 1996-300286	19960115
EP 722941	A3	20000412		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
US 5576321	A	19961119	US 1995-468900	19950606
PRAI US 1995-373823	A	19950117		
US 1995-468900	A	19950606		

OS MARPAT 125:168021
GI



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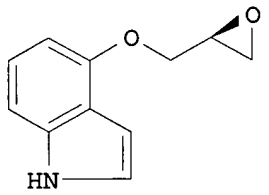
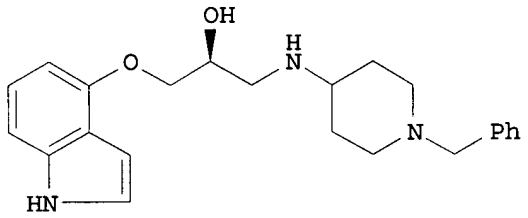


II



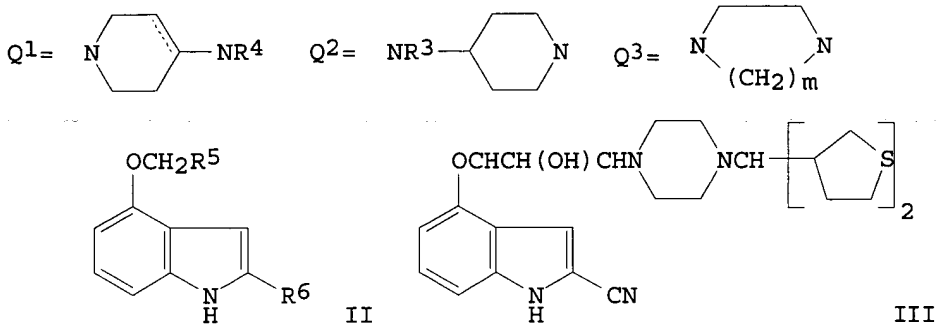
III

AB The title compds. [I; r = 0-4; s = 0-1; D = pyrrolo, imidazo, etc.; X = H, Ph; R = piperazino, piperidinyl, morpholino, etc.], useful for alleviating the symptoms of nicotine and tobacco withdrawal, and for the treatment of depression, anxiety, hypertension, etc., were prepd. and formulated. Thus, refluxing of indole II with 4-amino-1-benzylpiperidine in MeOH for 18 h afforded 78% desired product III. In general, compds. I are effective at 20-25 mg/day.

L10 ANSWER 17 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 1987:84635 CAPLUS
DN 106:84635
TI (Aryloxy)hydroxypropyl heterocycles
IN Berthold, Richard; Ott, Hans
PA Sandoz-Patent-G.m.b.H., Fed. Rep. Ger.
SO Ger. Offen., 60 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI DE 3524955	A1	19860130	DE 1985-3524955	19850712
GB 2163150	A1	19860219	GB 1985-17068	19850705
GB 2163150	B2	19880525		
CH 665208	A	19880429	CH 1985-2985	19850710
BE 902897	A1	19860115	BE 1985-11297	19850715
JP 61037765	A2	19860222	JP 1985-160011	19850718
PRAI DE 1984-3426630		19840719		

DE 1984-3426632 19840719
DE 1985-3509557 19850316
OS CASREACT 106:84635
GI



AB R1OCH2CH(OH)CH2Z(CO)nR2 [I; R1 = (un)substituted (hetero)aryl; R2 = (hetero)aryl, cycloalkyl, substituted alkyl; Z = NR3(CH2)nNR4, Q1, Q2, Q3; R3 = H, alkyl; R4 = H, alkyl, (un)substituted Ph; n = 0, 1 m = 2-4] were prepd. as cardiotonics (no data). Thus, (S)-2,2-dimethyl-1,3-dioxolane-4-methanol was sequentially benzylated deketalized, tosylated, and condensed with 4-hydroxy-1H-indole-2-carboxamide to give (R)-4-propoxyindole II [R5 = PhCH2OCH2CH(OH), R6 = CONH2]. This was debenzylated, epoxidized, and dehydrated to give (S)-II (R5 = oxiranyl, R6 = cyano). The latter was condensed with 1-(di-3-thienylmethyl)piperazine to give (S)-(indolyloxy)hydroxypropylpiperazine III.

L10 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 1986:572505 CAPLUS
DN 105:172505
TI 3-Aminopropoxyaryl derivatives
IN Berthold, Richard; Ott, Hans
PA Sandoz S. A., Switz.
SO Fr. Demande, 57 pp.
CODEN: FRXXBL
DT Patent
LA French
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	FR 2567885	A1	19860124	FR 1985-10852	19850712
	FR 2567885	B1	19880916		
	GB 2163150	A1	19860219	GB 1985-17068	19850705
	GB 2163150	B2	19880525		
	CH 665208	A	19880429	CH 1985-2985	19850710
	BE 902897	A1	19860115	BE 1985-11297	19850715
	JP 61037765	A2	19860222	JP 1985-160011	19850718
PRAI	DE 1984-3426630		19840719		
	DE 1984-3426632		19840719		
	DE 1985-3509557		19850316		

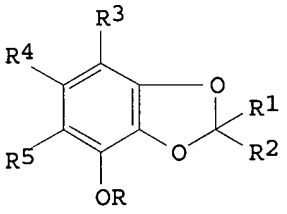
AB The title compds. R1OCH2CH(OH)CH2Z(CO)mR [R = (un)substituted alkyl; R1 = arom. or heteroarom. radical; Z = piperidinylamino, 4-piperazinylamino, NR2(CH2)nNR3; R2, R3 = H, alkyl; n = 2-4] are prepd. as cardiotonic, antiarrhythmic, and .alpha.- and .beta.-sympatholytics. Thus, melting a mixt. of (S)-4-(2,3-epoxypropoxy)-1H-indole-2-carbonitrile (prepn. given) with 1-(3,3'-dithienylmethyl)piperazine (prepn. given) gave (S)-4-[3-[4-(3,3'-dithienylmethyl)piperazin-1-yl]-2-hydroxypropoxy]-1H-indole-2-carbonitrile (I). I (10-9-10-6M) inhibited the pos. inotropic

effect of adrenaline on the guinea pig auricle, in vitro.

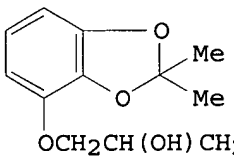
L10 ANSWER 19 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 1984:139086 CAPLUS
DN 100:139086
TI Ring-substituted pyrogallol derivatives
IN Schlager, Ludwig H.
PA Gerot-Pharmazeutika G.m.b.H., Austria
SO Eur. Pat. Appl., 38 pp.
CODEN: EPXXDW
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 95454	A2	19831130	EP 1983-890068	19830502
	EP 95454	A3	19850403		
	R: BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	AT 8201888	A	19840115	AT 1982-1888	19820513
	AT 375654	B	19840827		
	AT 8204671	A	19831215	AT 1982-4671	19821223
	AT 375360	B	19840725		
	AT 8301298	A	19841115	AT 1983-1298	19830412
	AT 378191	B	19850625		
	CA 1233181	A1	19880223	CA 1983-427476	19830504
	AU 8314409	A1	19831117	AU 1983-14409	19830510
	AU 566107	B2	19871008		
	DK 8302104	A	19831114	DK 1983-2104	19830511
	NO 8301680	A	19831114	NO 1983-1680	19830511
	CS 235321	B2	19850515	CS 1983-3308	19830511
	PL 141325	B1	19870731	PL 1983-241918	19830511
	JP 58206581	A2	19831201	JP 1983-81827	19830512
	DD 209831	A5	19840523	DD 1983-250870	19830512
	DD 209831	C4	19851218		
	HU 33092	O	19841029	HU 1983-1658	19830512
	CS 235344	B2	19850515	CS 1984-142	19840105
PRAI	AT 1982-1888		19820513		
	AT 1982-4671		19821223		
	AT 1983-1298		19830412		
	CS 1983-3308		19830511		

OS CASREACT 100:139086
GI



I



$OCH_2CH(OH)CH_2NCMe_3$ II

AB 3-Benzodioxolyl ethers I [R = H, aminohydroxyalkyl, carboxyalkyl, etc.; R1, R2 = H or lower alkyl; at least one of R3-5 = halo or NO2] were prepd. as analgesics and .beta.-sympatholytics. Thus, 2,2-dimethyl-1,3-benzodioxol-4-ol was treated with epichlorohydrin, then Me3CNH2 to give the amino alc. ether II, which was superior to Atenolol as a .beta.-blocker and a more effective analgesic than, e.g., pethidine-HCl.

AN 2002:72070 CAPLUS
DN 136:134677
TI Substituted 2-(S)-hydroxy-3-[(piperidin-4-yl-methyl)amino]propyl ethers and substituted 2-aryl-2-(R)-hydroxy-1-(piperidin-4-yl-methyl)ethylamines as beta-3 adrenergic receptor agonists, antidiabetics, and antiobesity agents
IN Steffan, Robert John; Ashwell, Mark Anthony; Pelletier, Jeffrey Claude; Solvibile, William Ronald; Matelan, Edward Martin
PA American Home Products Corporation, USA
SO PCT Int. Appl., 216 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002006255	A2	20020124	WO 2001-US22363	20010716
WO 2002006255	A3	20020321		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2002037907	A1	20020328	US 2001-903738	20010712
US 6506901	B2	20030114		
PRAI US 2000-218753P	P	20000717		

OS MARPAT 136:134677
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention provides title compds. I and their pharmaceutically acceptable salts [wherein A = OCH2, bond; R = (un)substituted aryl or certain N/O/S heterocyclyl; R1 = (cyclo)alkyl, alkoxy, (cyclo)alkylamino, (un)substituted aryl, arylamino, arylalkyl, or heterocyclyl; Z = bond, SO2, CO]. I are useful in treating or inhibiting metabolic disorders related to insulin resistance or hyperglycemia (typically assocd. with obesity or glucose intolerance), atherosclerosis, gastrointestinal disorders, neurogenic inflammation, glaucoma, ocular hypertension, and frequent urination. The compds. are particularly useful in the treatment or inhibition of type II diabetes. They are also useful for increasing lean meat deposition and/or increasing the lean meat to fat ratio in animals, particularly mammals. Approx. 240 individual compds. and addnl. salts were prepd. by either std. or combinatorial methods. For instance, invention compd. II was prepd. by reaction of the (S)-isomeric epoxide III with the corresponding amine. II had an EC50 of 0.001 .mu.M against cloned human .beta.3 adrenoceptors in vitro, with a maximal response comparable to isoproterenol.

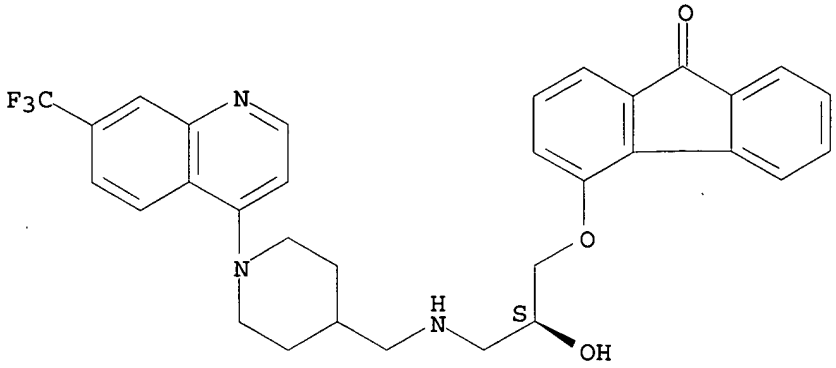
IT **392688-10-7P**, 4-[[(2S)-2-Hydroxy-3-[[[1-(7-trifluoromethylquinolin-4-yl)piperidin-4-yl]methyl]amino]propyl]oxy]fluoren-9-one
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; prepn. of piperidine hydroxyaminopropyl ether and hydroxyethylamine derivs. as .beta.3 adrenergic receptor agonists,

antidiabetics, and antiobesity agents)

RN 392688-10-7 CAPLUS

CN 9H-Fluoren-9-one, 4-[(2S)-2-hydroxy-3-[[[1-[7-(trifluoromethyl)-4-quinolinyl]-4-piperidinyl]methyl]amino]propoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

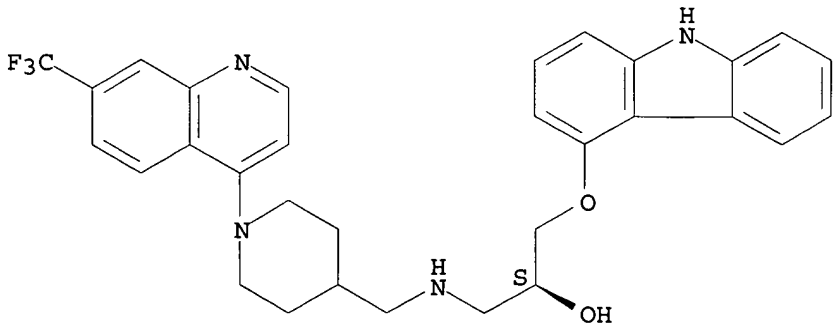


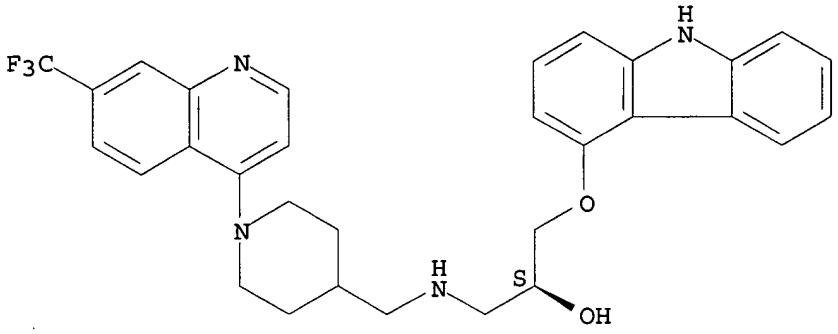
IT **392688-07-2P**, (2S)-1-(9H-Carbazol-4-yloxy)-3-[[[1-(7-trifluoromethylquinolin-4-yl)piperidin-4-yl]methyl]amino]propan-2-ol **392688-09-4P**, (2S)-1-(4-Benzyloxyphenoxy)-3-[[[1-(7-trifluoromethylquinolin-4-yl)piperidin-4-yl]methyl]amino]propan-2-ol **392688-11-8P**, 4-[[(2S)-2-Hydroxy-3-[[[1-(7-trifluoromethylquinolin-4-yl)piperidin-4-yl]methyl]amino]propyl]oxy]fluoren-9-one oxime **392688-12-9P**, (2S)-1-(9H-Carbazol-4-yloxy)-3-[[(4'-trifluoromethyl-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-yl)methyl]amino]propan-2-ol **392688-13-0P**, 4-[[(2S)-2-Hydroxy-3-[[(4'-trifluoromethyl-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-yl)methyl]amino]propyl]oxy]fluoren-9-one **392688-14-1P**, 1-[[(2S)-2-Hydroxy-3-[[(4'-trifluoromethyl-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-yl)methyl]amino]propyl]oxy]fluoren-9-one **392692-26-1P**, (2S)-1-(9H-Carbazol-4-yloxy)-3-[[[1-(7-trifluoromethylquinolin-4-yl)piperidin-4-yl]methyl]amino]propan-2-ol dihydrochloride **392692-27-2P**, 4-[[(2S)-2-Hydroxy-3-[[[1-(7-trifluoromethylquinolin-4-yl)piperidin-4-yl]methyl]amino]propyl]oxy]fluoren-9-one oxime dihydrochloride
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; prepn. of piperidine hydroxyaminopropyl ether and hydroxyethylamine derivs. as .beta.3 adrenergic receptor agonists, antidiabetics, and antiobesity agents)

RN 392688-07-2 CAPLUS

CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[[1-[7-(trifluoromethyl)-4-quinolinyl]-4-piperidinyl]methyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

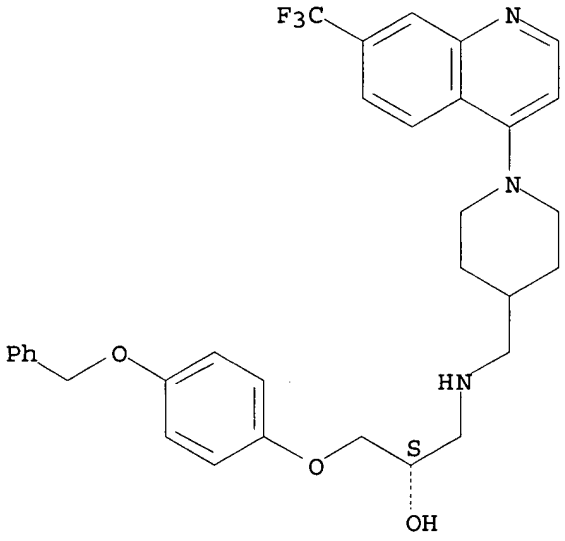
Absolute stereochemistry.





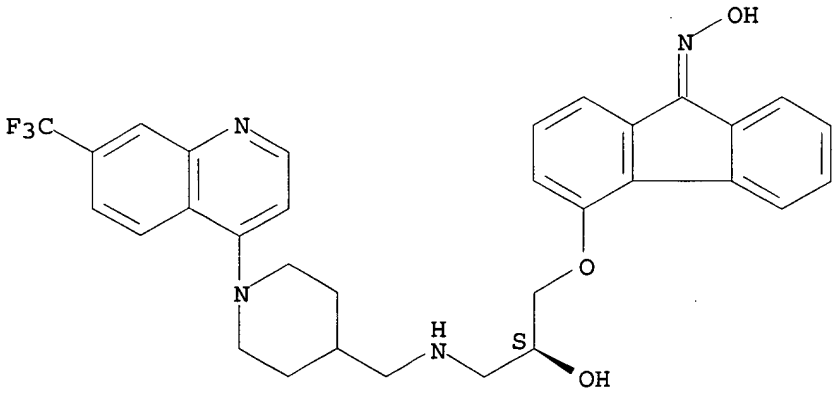
RN 392688-09-4 CAPLUS
CN 2-Propanol, 1-[4-(phenylmethoxy)phenoxy]-3-[[[1-[7-(trifluoromethyl)-4-quinolinyl]-4-piperidinyl]methyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

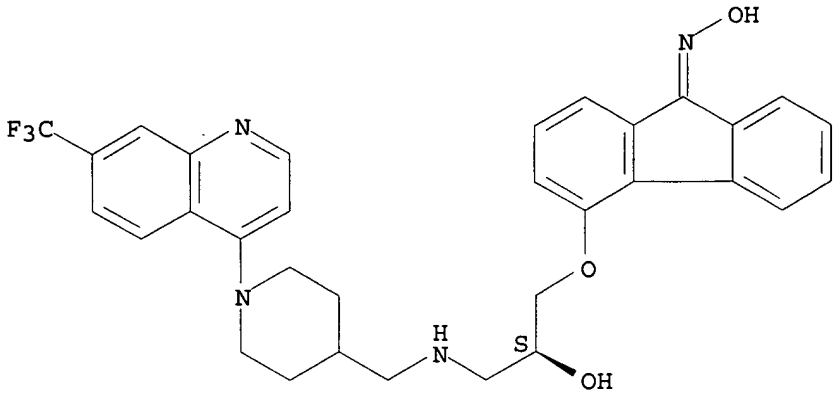
Absolute stereochemistry.



RN 392688-11-8 CAPLUS
CN 9H-Fluoren-9-one, 4-[(2S)-2-hydroxy-3-[[[1-[7-(trifluoromethyl)-4-quinolinyl]-4-piperidinyl]methyl]amino]propoxy]-, oxime (9CI) (CA INDEX NAME)

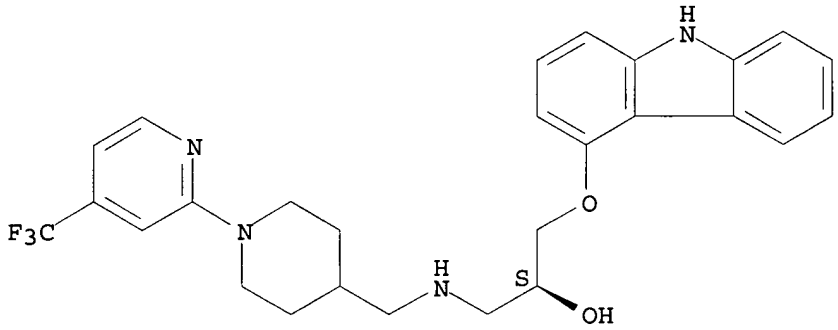
Absolute stereochemistry.
Double bond geometry unknown.





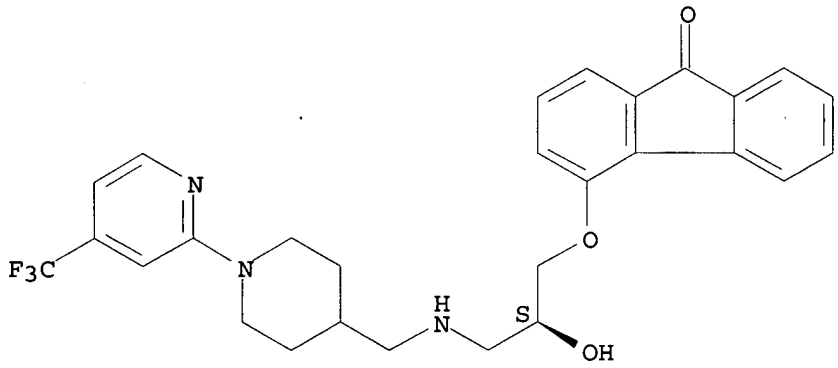
RN 392688-12-9 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[[1-[4-(trifluoromethyl)-2-pyridinyl]-4-piperidinyl]methyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



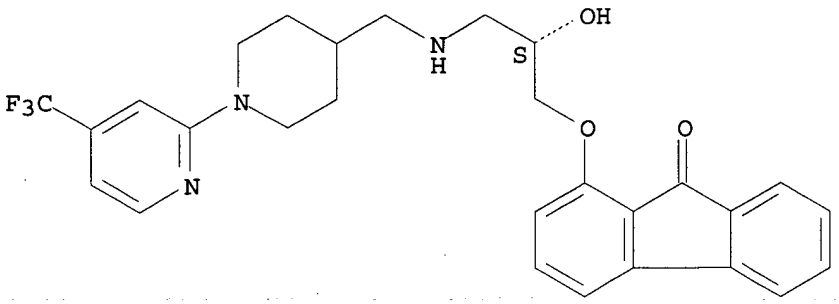
RN 392688-13-0 CAPLUS
CN 9H-Fluoren-9-one, 4-[(2S)-2-hydroxy-3-[[[1-[4-(trifluoromethyl)-2-pyridinyl]-4-piperidinyl]methyl]amino]propoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



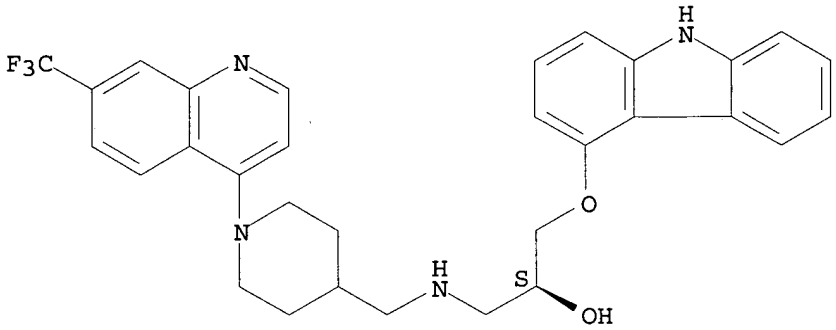
RN 392688-14-1 CAPLUS
CN 9H-Fluoren-9-one, 1-[(2S)-2-hydroxy-3-[[[1-[4-(trifluoromethyl)-2-pyridinyl]-4-piperidinyl]methyl]amino]propoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 392692-26-1 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[[1-[7-(trifluoromethyl)-4-quinolinyl]-4-piperidinyl]methyl]amino]-, dihydrochloride, (2S)- (9CI) (CA INDEX NAME)

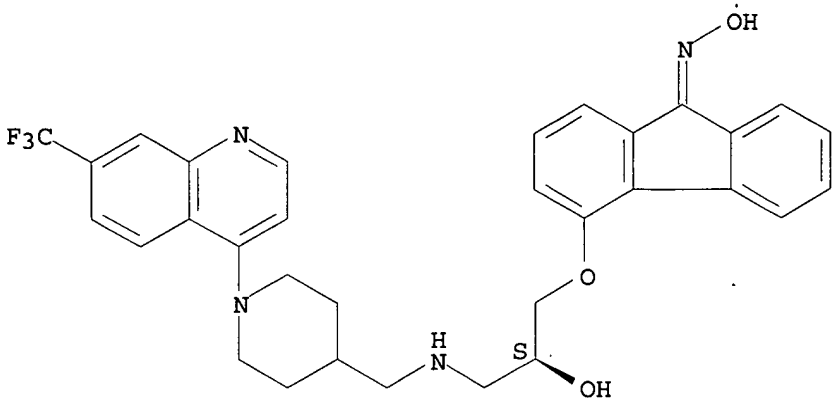
Absolute stereochemistry.



●2 HCl

RN 392692-27-2 CAPLUS
CN 9H-Fluoren-9-one, 4-[(2S)-2-hydroxy-3-[[[1-[7-(trifluoromethyl)-4-quinolinyl]-4-piperidinyl]methyl]amino]propoxy]-, oxime, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



● 2 HCl

AN 2002:72089 CAPLUS
DN 136:134678
TI Preparation of [(2-hydroxyethylamino)cyclylamino]arylsulfonamides as .beta.3 adrenergic receptor agonists
IN Sum, Fuk-Wah; Malamas, Michael Sotirios
PA American Home Products Corporation, USA
SO PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002006274	A1	20020124	WO 2001-US22379	20010716
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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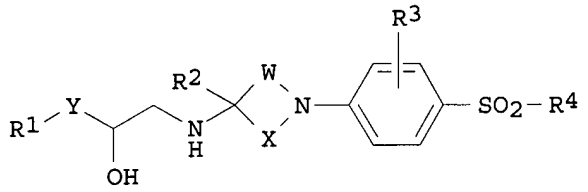
	US 2002028797	A1	20020307	US 2001-904114	20010712
	US 6444685	B2	20020903		
	US 2003027795	A1	20030206	US 2002-205019	20020725
PRAI	US 2000-218589P	P	20000717		
	US 2001-904114	A3	20010712		

OS MARPAT 136:134678
GI



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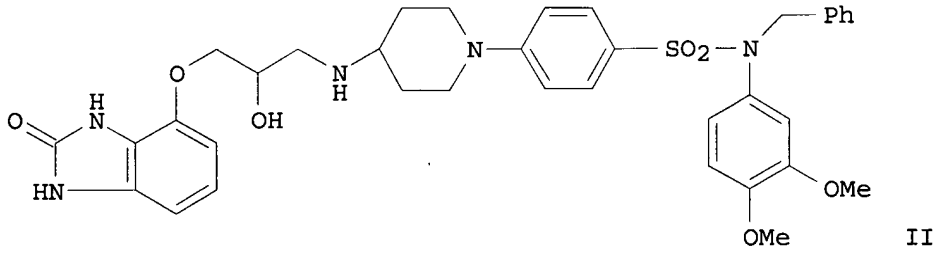


II

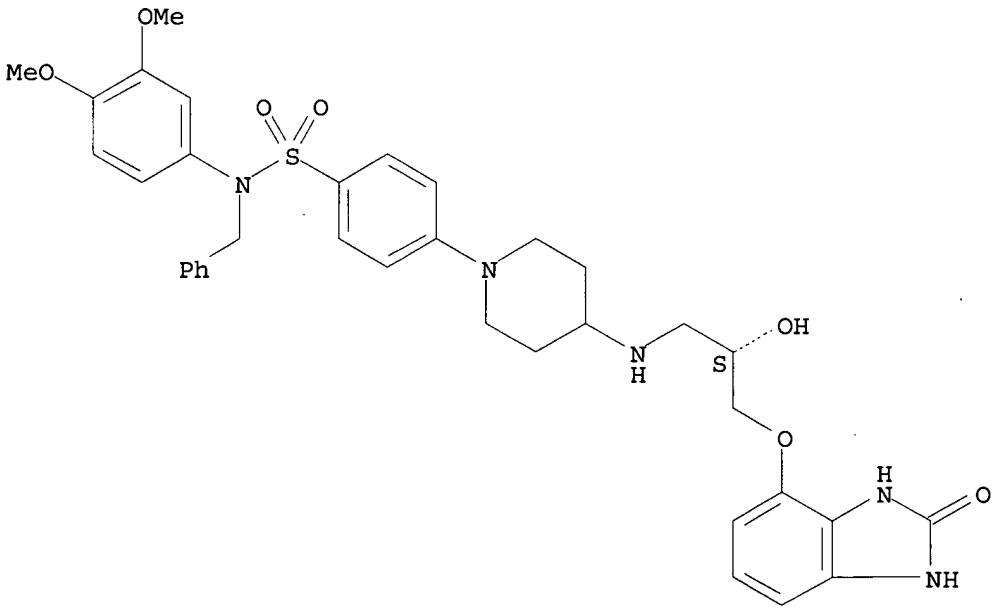
AB Title compds. I [wherein W = (CH2)m; X = (CH2)n; m = 1-3; n = 1-3; Y = OCH2, SCH2, or a bond; R1 = Ph, heterocyclyl, or heteroaryl substituted with R5 or R6; R2 = H, CF3, alkyl, alkenyl, or alkynyl; R4 = (cyclo)alkyl, alkenyl, alkynyl, OH, alkoxy, (hetero)aryloxy, (hetero)arylamino, alkoxycarbonylalkyl, carboxyalkyl, aminosulfonylalkyl, alkylsulfonylalkyl, or (un)substituted Ph, heterocyclyl, heteroaryl, acylamino, amino, etc.; R3, R5, and R6 = independently H, CF3, (cyclo)alkyl, alkenyl, alkynyl, aryl, heterocyclyl, heteroaryl, arylalkyl, halo, CN, NO2, OH, alkoxy, (hetero)aryloxy, alkylthio, arylthio, (hetero)arylamino, alkylcarbonylalkyl, aminosulfonylalkyl, arylsulfonylalkyl, etc.; or a

pharmaceutically acceptable salt thereof] were prepd. as .beta.3 adrenergic receptor agonists. For example, sodium triacetoxyborohydride was added to a soln. of 4-[(2S)-3-amino-2-hydroxypropoxy]-1,3-dihydrobenzimidazol-2-one, N-benzyl-N-(3,4-dimethoxyphenyl)-4-(4-oxopiperidin-1-yl)sulfonamide, and AcOH in anhyd. DMF. The reaction was stirred overnight and then quenched with 50% H2O/satd. NaHCO3 to give II. The latter exhibited selective binding to the .beta.3 adrenergic receptor (EC50 0.017 .mu.M) compared to the .beta.1 and .beta.2 adrenergic receptors. Thus, I are useful in treating metabolic disorders related to insulin resistance or hyperglycemia (typically assocd. with obesity or glucose intolerance), atherosclerosis, gastrointestinal disorders, neurogenetic inflammation, glaucoma, ocular hypertension, and frequent urination, and are particularly useful in the treatment of type II diabetes.

IT **391934-05-7P 391934-06-8P 391934-08-0P**
391934-10-4P 391934-11-5P 391934-13-7P
391934-14-8P 391934-15-9P 391934-16-0P
391934-17-1P 391934-20-6P 391934-21-7P
391934-50-2P 391934-53-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(.beta.3 agonist; prepn. of [(hydroxyethylamino)piperidinyl]benzenesulfonamides as .beta.3 adrenergic receptor agonists for treatment of metabolic disorders related to insulin resistance or hyperglycemia)

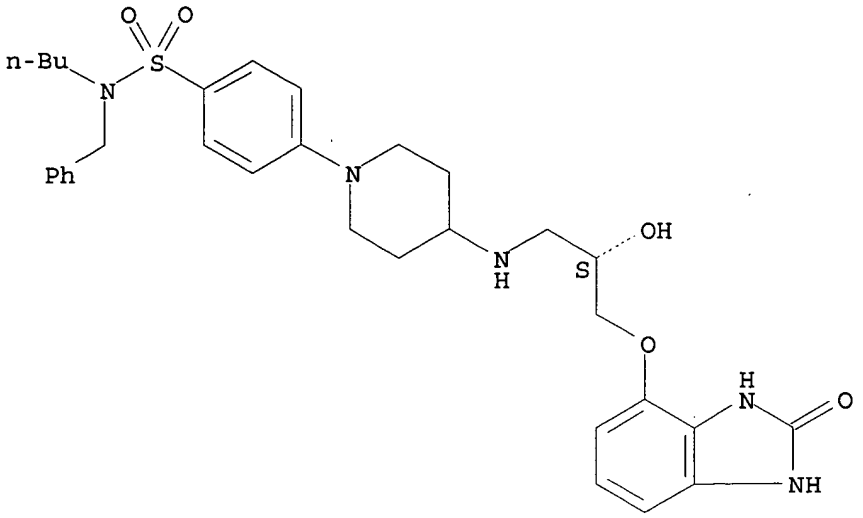
RN 391934-05-7 CAPLUS
CN Benzenesulfonamide, 4-[4-[[(2S)-3-[(2,3-dihydro-2-oxo-1H-benzimidazol-4-yl)oxy]-2-hydroxypropyl]amino]-1-piperidinyl]-N-(3,4-dimethoxyphenyl)-N-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



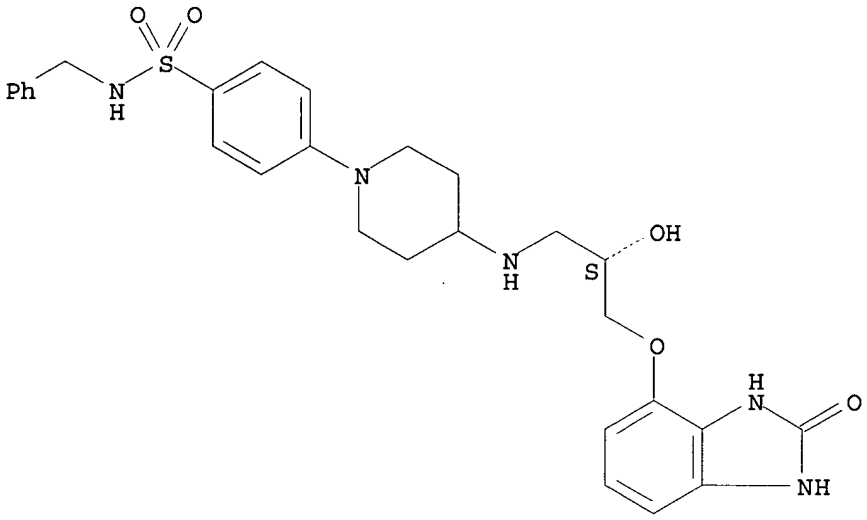
RN 391934-06-8 CAPLUS
CN Benzenesulfonamide, N-butyl-4-[4-[[(2S)-3-[(2,3-dihydro-2-oxo-1H-benzimidazol-4-yl)oxy]-2-hydroxypropyl]amino]-1-piperidinyl]-N-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



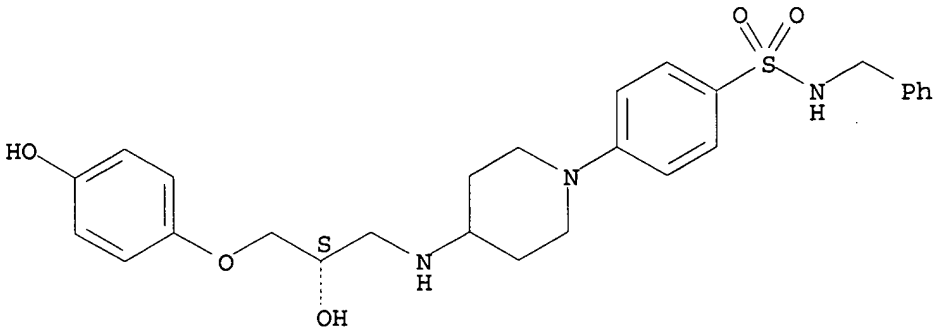
RN 391934-08-0 CAPLUS
CN Benzenesulfonamide, 4-[4-[[(2S)-3-[(2,3-dihydro-2-oxo-1H-benzimidazol-4-yl)oxy]-2-hydroxypropyl]amino]-1-piperidinyl]-N-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



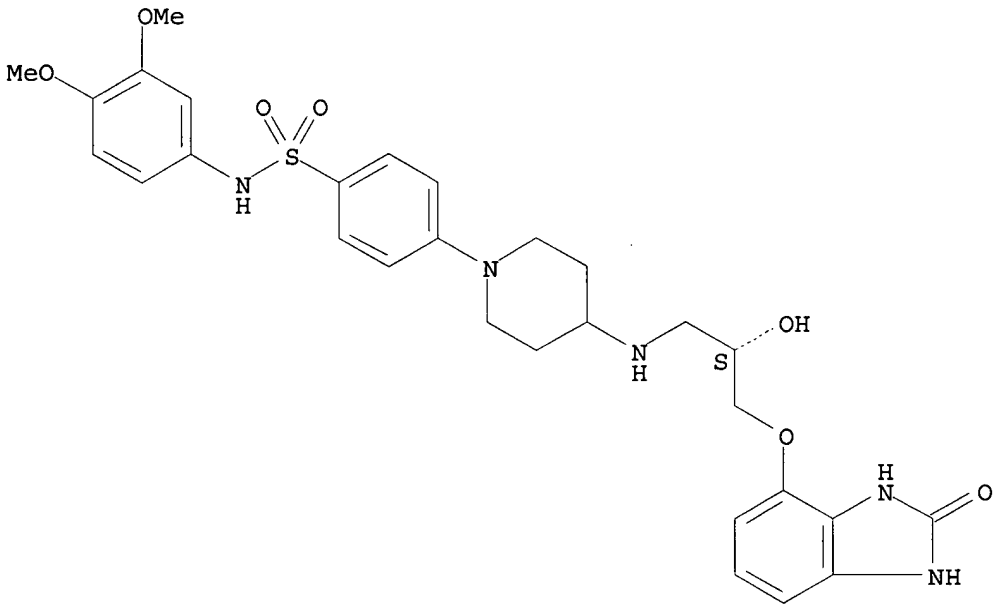
RN 391934-10-4 CAPLUS
CN Benzenesulfonamide, 4-[4-[[(2S)-2-hydroxy-3-(4-hydroxyphenoxy)propyl]amino]-1-piperidinyl]-N-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 391934-11-5 CAPLUS
CN Benzenesulfonamide, 4-[4-[[(2S)-3-[(2,3-dihydro-2-oxo-1H-benzimidazol-4-yl)oxy]-2-hydroxypropyl]amino]-1-piperidinyl]-N-(3,4-dimethoxyphenyl)- (9CI) (CA INDEX NAME)

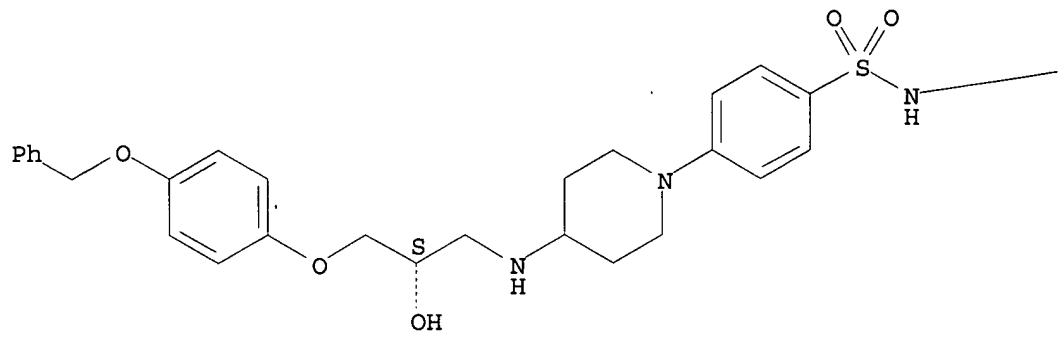
Absolute stereochemistry.



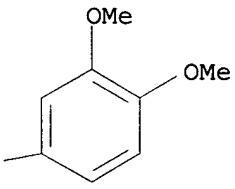
RN 391934-13-7 CAPLUS
CN Benzenesulfonamide, N-(3,4-dimethoxyphenyl)-4-[4-[[(2S)-2-hydroxy-3-[4-(phenylmethoxy)phenoxy]propyl]amino]-1-piperidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

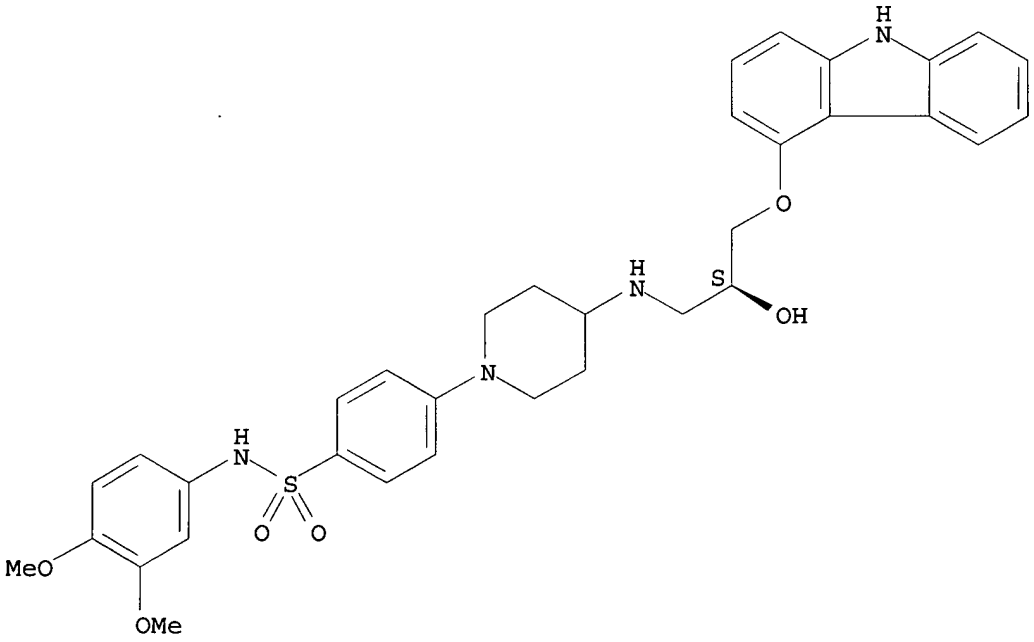


PAGE 1-B



RN 391934-14-8 CAPLUS
CN Benzenesulfonamide, 4-[4-[[(2S)-3-(9H-carbazol-4-yloxy)-2-hydroxypropyl]amino]-1-piperidinyl]-N-(3,4-dimethoxyphenyl)- (9CI) (CA INDEX NAME)

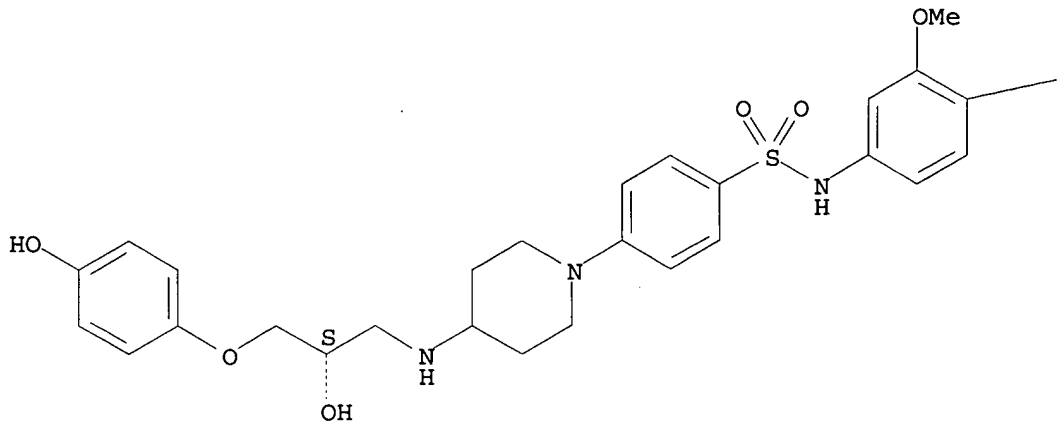
Absolute stereochemistry.



RN 391934-15-9 CAPLUS
CN Benzenesulfonamide, N-(3,4-dimethoxyphenyl)-4-[4-[[(2S)-2-hydroxy-3-(4-hydroxyphenoxy)propyl]amino]-1-piperidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

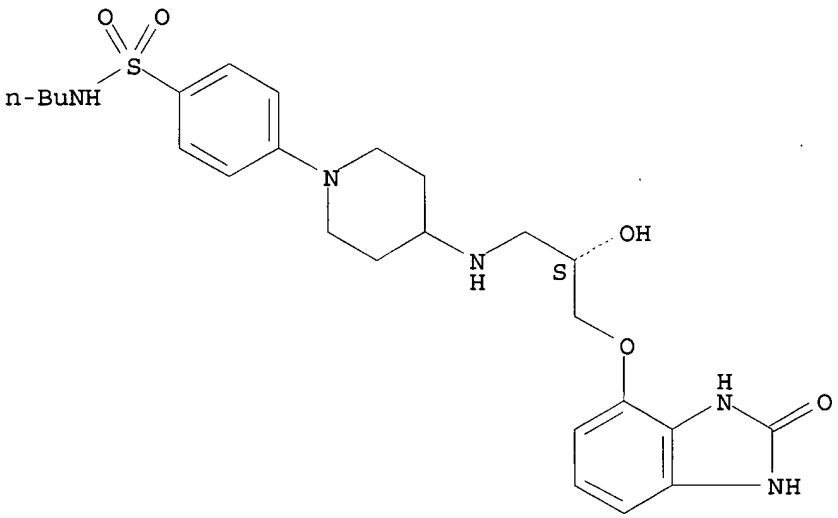


PAGE 1-B

—OMe

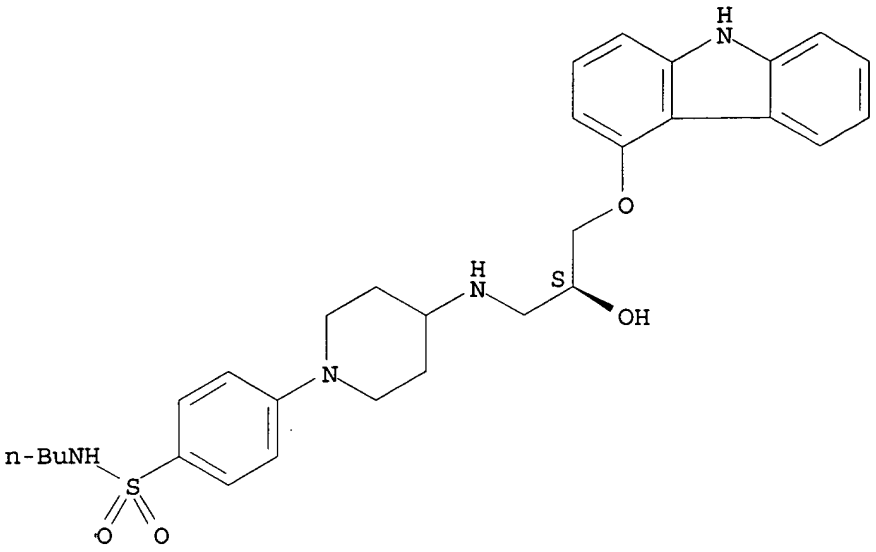
RN 391934-16-0 CAPLUS
CN Benzenesulfonamide, N-butyl-4-[4-[[(2S)-3-[(2,3-dihydro-2-oxo-1H-benzimidazol-4-yl)oxy]-2-hydroxypropyl]amino]-1-piperidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



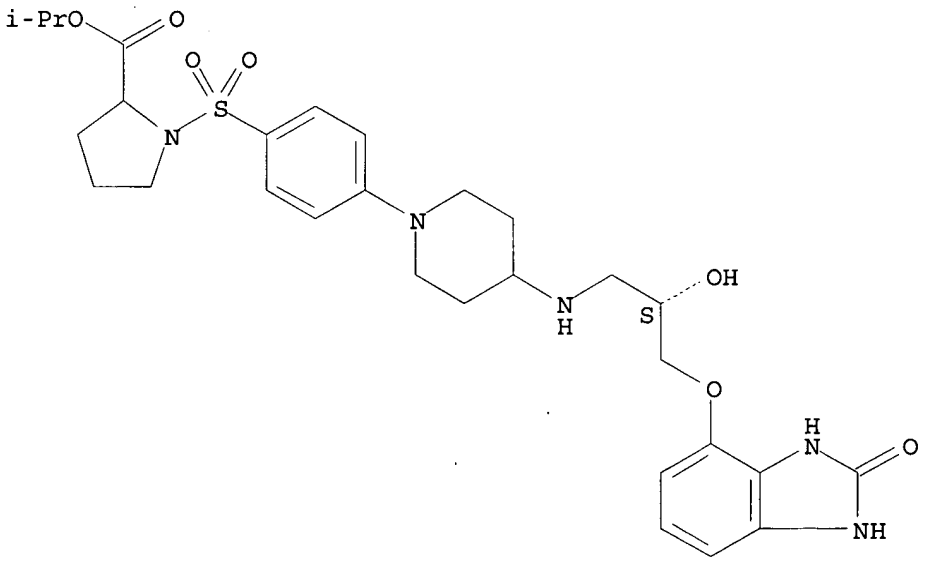
RN 391934-17-1 CAPLUS
CN Benzenesulfonamide, N-butyl-4-[4-[[(2S)-3-(9H-carbazol-4-yloxy)-2-hydroxypropyl]amino]-1-piperidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



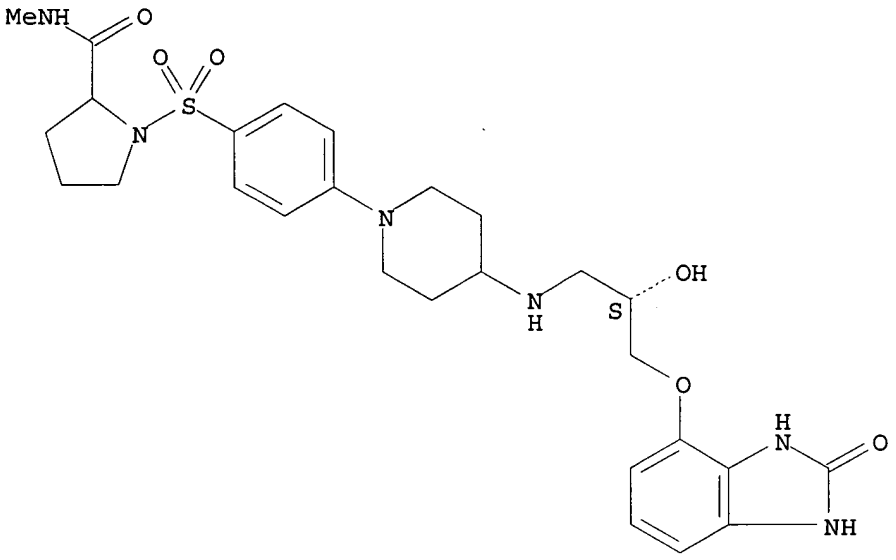
RN 391934-20-6 CAPLUS
CN Proline, 1-[[4-[4-[[(2S)-3-[(2,3-dihydro-2-oxo-1H-benzimidazol-4-yl)oxy]-2-hydroxypropyl]amino]-1-piperidinyl]phenyl]sulfonyl]-, 1-methylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



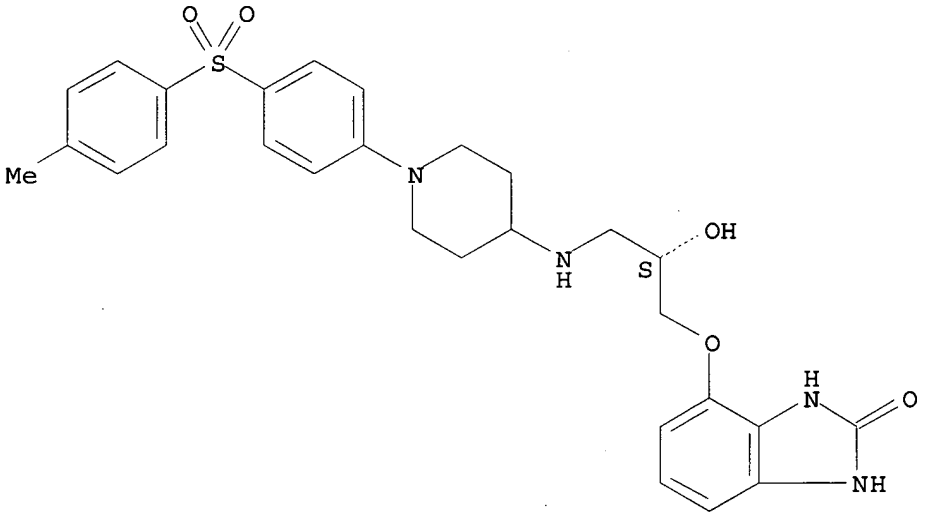
RN 391934-21-7 CAPLUS
CN 2-Pyrrolidinecarboxamide, 1-[[4-[4-[[(2S)-3-[(2,3-dihydro-2-oxo-1H-benzimidazol-4-yl)oxy]-2-hydroxypropyl]amino]-1-piperidinyl]phenyl]sulfonyl]-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



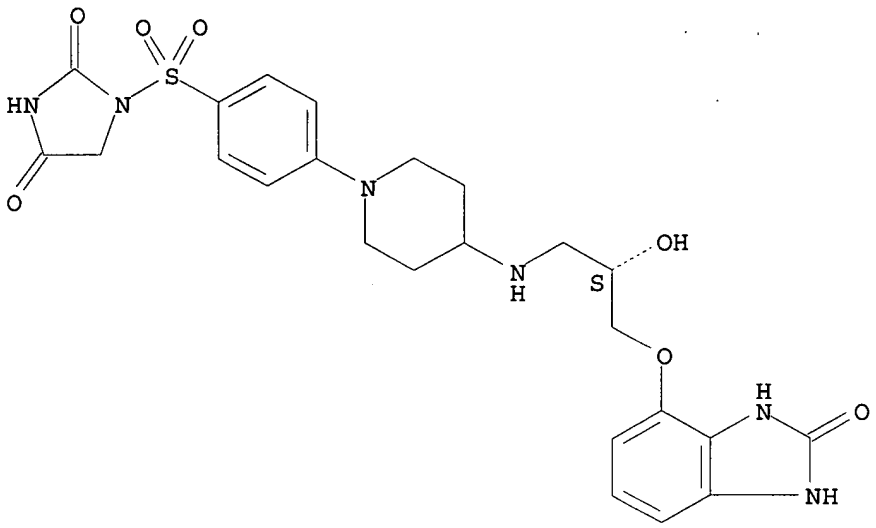
RN 391934-50-2 CAPLUS
CN 2H-Benzimidazol-2-one, 1,3-dihydro-4-[(2S)-2-hydroxy-3-[[1-[4-[(4-methylphenyl)sulfonyl]phenyl]-4-piperidinyl]amino]propoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 391934-53-5 CAPLUS
CN 2,4-Imidazolidinedione, 1-[[4-[4-[[(2S)-3-[(2,3-dihydro-2-oxo-1H-benzimidazol-4-yl)oxy]-2-hydroxypropyl]amino]-1-piperidinyl]phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AN 2002:72096 CAPLUS
DN 136:134754
TI 2-Substituted thiazolidinones as beta-3 adrenergic receptor agonists, useful as antidiabetics and antiobesity agents
IN Hu, Baihua
PA American Home Products Corporation, USA
SO PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002006281	A1	20020124	WO 2001-US22526	20010716
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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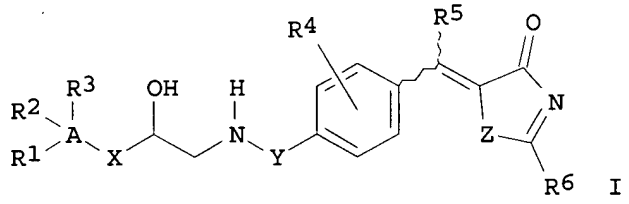
	US 2002169325	A1	20021114	US 2002-132483	20020425
PRAI	US 2000-218724P	P	20000717		
	US 2001-904157	A3	20010712		

OS MARPAT 136:134754
GI



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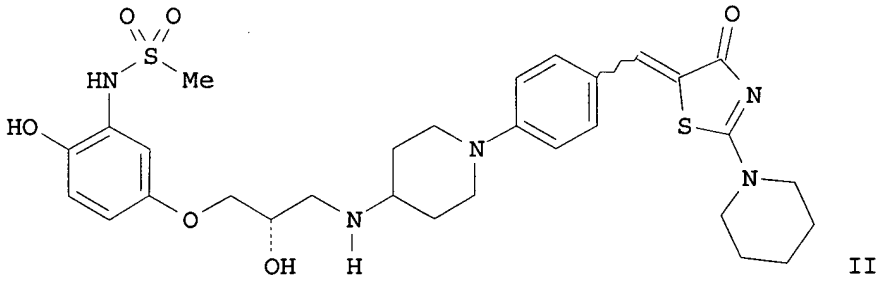


II

AB The invention provides compds. I or their pharmaceutically acceptable salts [A = aryl or selected heterocyclyl; X = OCH2, SCH2, or bond; Y = alkyl, alkoxy, azetidine, pyrrolidine, or piperidine (latter 3 attached to Ph via N atom); Z = S, O, NH, or N-alkyl; R1, R2, R3 = H, alkyl, cycloalkyl, OH, halo, CF3, alkoxy, PhCH2O, allyloxy, propargyloxy, acyloxy, cyano, NO2, (un)substituted amino, or 2 of these 3 substituents can combine to form an aryl-fused cycloalkyl optionally substituted by acylamino or OH; R4 = H, alkyl, alkoxy, OH, CO2H, or halo; R5 = H, alkyl; R6 = SCH3, (un)substituted NH2, amino acid or ester thereof (attached at

amino), NHCONH2 or derivs., NHNHCONH2 or derivs.]. The compds. are selective .beta.3 adrenergic receptor agonists, useful in treating or inhibiting metabolic disorders related to insulin resistance or hyperglycemia (typically assocd. with obesity or glucose intolerance), atherosclerosis, gastrointestinal disorders, neurogenic inflammation, and frequent urination, and are particularly useful in the treatment or inhibition of type II diabetes. The compds. are also useful as feed additives, for increasing lean meat deposition and/or the ratio of lean meat to fat in animals, particularly mammals. Examples include 34 invention compd. syntheses and 38 intermediate prepns. For instance, N-benzyl-N-(2-benzyloxy-5-hydroxyphenyl)methanesulfonamide was etherified with (2S)-(+)-glycidyl 3-nitrobenzenesulfonate, and the resultant epoxide was aminated with dibenzylamine and hydrogenated to give N-[5-[((2S)-3-amino-2-hydroxypropyl)oxy]-2-hydroxyphenyl]methanesulfonamide. Reductive amination of a corresponding piperidinone deriv. by the latter compd. gave invention compd. II. This compd. bound to cloned human .beta.3 adrenoceptors in vitro with EC50 of 1 nM, and a maximal response comparable to isoproterenol.

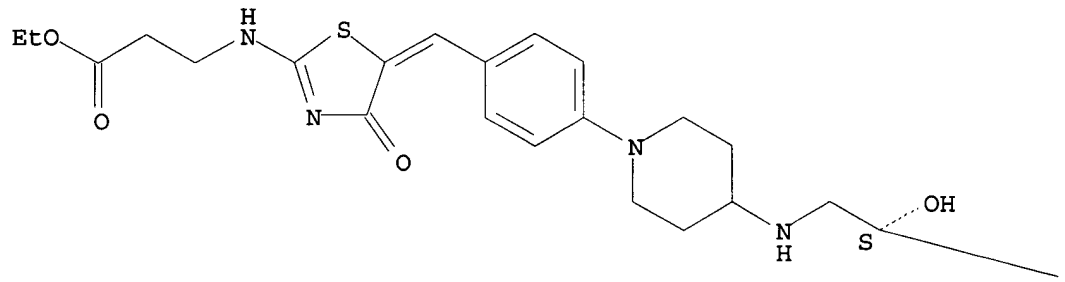
IT **391872-57-4P**, 3-[[5-[4-[4-[[(2S)-2-Hydroxy-3-([2-oxo-2,3-dihydro-1H-benzimidazol-4-yl]oxy)propyl]amino]piperidin-1-yl]benzylidene]-4-oxo-4,5-dihydrothiazol-2-yl]amino]propionic acid ethyl ester
RL: FFD (Food or feed use); PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; prepn. of thiazolidinone derivs. as .beta.3 adrenergic receptor agonists, antidiabetics, and antiobesity agents)

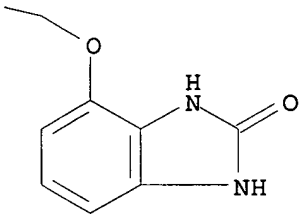
RN 391872-57-4 CAPLUS

CN .beta.-Alanine, N-[5-[[4-[4-[[(2S)-3-[(2,3-dihydro-2-oxo-1H-benzimidazol-4-yl)oxy]-2-hydroxypropyl]amino]-1-piperidinyl]phenyl]methylene]-4,5-dihydro-4-oxo-2-thiazolyl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



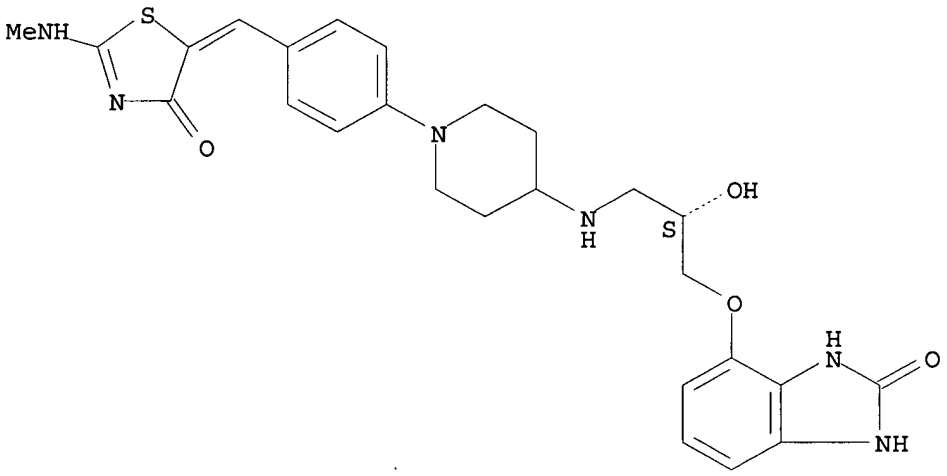


IT **391872-50-7P**, 4-[[(2S)-2-Hydroxy-3-[[1-[4-((2-(methylamino)-4-oxo-4H-thiazol-5-ylidene)methyl)phenyl]piperidin-4-yl]amino]propyl]oxy]-1,3-dihydrobenzimidazol-2-one **391872-51-8P**, 4-[[(2S)-2-Hydroxy-3-[[1-[4-[[2-[[2-(morpholin-4-yl)ethyl]amino)-4-oxo-4H-thiazol-5-ylidene]methyl]phenyl]piperidin-4-yl]amino]propyl]oxy]-1,3-dihydrobenzimidazol-2-one **391872-52-9P**, 4-[[(2S)-3-[[1-[4-[[2-[(1-Benzylpiperidin-4-yl]amino)-4-oxo-4H-thiazol-5-ylidene]methyl]phenyl]piperidin-4-yl]amino]-2-hydroxypropyl]oxy]-1,3-dihydrobenzimidazol-2-one **391872-53-0P**, 2-([1-Benzylpiperidin-4-yl]amino)-5-[4-[4-[[(2S)-2-hydroxy-3-(4-hydroxyphenoxy)propyl]amino]piperidin-1-yl]benzylidene]thiazol-4-one **391872-55-2P**, N'-[5-[4-[4-[[(2S)-2-Hydroxy-3-[(2-oxo-2,3-dihydro-1H-benzimidazol-4-yl)oxy]propyl]amino]piperidin-1-yl]benzylidene]-4-oxo-4,5-dihydrothiazol-2-yl]-N,N-dimethylguanidine **391872-58-5P**, 3-[[5-[4-[4-[[(2S)-2-Hydroxy-3-([2-oxo-2,3-dihydro-1H-benzimidazol-4-yl]oxy)propyl]amino]piperidin-1-yl]benzylidene]-4-oxo-4,5-dihydrothiazol-2-yl]amino]propionic acid **391872-59-6P**, 4-[[(2S)-2-Hydroxy-3-[[1-[4-[(2-[hydroxyamino]-4-oxo-4H-thiazol-5-ylidene]methyl)phenyl]piperidin-4-yl]amino]propyl]oxy]-1,3-dihydrobenzimidazol-2-one **391872-61-0P**, 4-[[(2S)-2-Hydroxy-3-[[1-[4-[(4-oxo-2-[piperidin-1-yl]-4H-thiazol-5-ylidene]methyl)phenyl]piperidin-4-yl]amino]propyl]oxy]-1,3-dihydrobenzimidazol-2-one **391872-63-2P**, N-[2-Hydroxy-5-[[(2S)-2-hydroxy-3-[[1-[4-[(4-oxo-2-[piperidin-1-yl]-4H-thiazol-5-ylidene]methyl)phenyl]piperidin-4-yl]amino]propyl]oxy]phenyl]methanesulfonamide **391872-64-3P**, 8-Hydroxy-5-[[(2S)-2-hydroxy-3-[[1-[4-[(4-oxo-2-[piperidin-1-yl]-4H-thiazol-5-ylidene]methyl)phenyl]piperidin-4-yl]amino]propyl]oxy]-3,4-dihydro-1H-quinolin-2-one **391872-65-4P**, 5-[4-[4-[[(2S)-2-Hydroxy-3-(4-hydroxyphenoxy)propyl]amino]piperidin-1-yl]benzylidene]-2-[piperidin-1-yl]thiazol-4-one **391872-66-5P**, N'-[5-[4-[4-[[(2S)-2-Hydroxy-3-([8-hydroxy-2-oxo-1,2,3,4-tetrahydroquinolin-5-yl]oxy)propyl]amino]piperidin-1-yl]benzylidene]-4-oxo-4,5-dihydrothiazol-2-yl]-N,N-dimethylguanidine **391872-67-6P** **391872-68-7P**, 4-[[(2S)-2-Hydroxy-3-[[1-[4-[[2-(4-methylpiperazin-1-yl)-4-oxo-4H-thiazol-5-ylidene]methyl]phenyl]piperidin-4-yl]amino]propyl]oxy]-1,3-dihydrobenzimidazol-2-one **391872-69-8P**, N'-[5-[4-[4-[((2S)-2-Hydroxy-3-phenoxypropyl]amino)piperidin-1-yl]benzylidene]-4-oxo-4,5-dihydrothiazol-2-yl]-N,N-dimethylguanidine **391872-70-1P**, N'-[5-[4-[4-[[(2S)-2-Hydroxy-3-(4-hydroxyphenoxy)propyl]amino]piperidin-1-yl]benzylidene]-4-oxo-4,5-dihydrothiazol-2-yl]-N,N-dimethylguanidine **391872-71-2P**, 5-[4-[4-[((2S)-2-Hydroxy-3-phenoxypropyl]amino)piperidin-1-yl]benzylidene]-2-morpholin-4-ylthiazol-4-one dihydrochloride **391872-72-3P**,

5-[4-[4-[[(2S)-2-Hydroxy-3-(4-hydroxyphenoxy)propyl]amino]piperidin-1-yl]benzylidene]-2-morpholin-4-ylthiazol-4-one **391872-73-4P**, 5-[4-[4-[[(2S)-2-Hydroxy-3-(4-hydroxyphenoxy)propyl]amino]piperidin-1-yl]benzylidene]-2-(4-methylpiperazin-1-yl)thiazol-4-one **391872-75-6P**, 2-[(3-[Dimethylamino]propyl]amino)-5-[4-[4-[((2S)-2-hydroxy-3-phenoxypropyl]amino)piperidin-1-yl]benzylidene]thiazol-4-one **391872-76-7P**, 2-Hexylamino-5-[4-[4-[((2S)-2-hydroxy-3-phenoxypropyl]amino)piperidin-1-yl]benzylidene]thiazol-4-one **391872-78-9P**, (2S)-2-[[5-[4-[4-[[(2S)-2-Hydroxy-3-[(2-oxo-2,3-dihydro-1H-benzimidazol-4-yl]oxy)propyl]amino]piperidin-1-yl]benzylidene]-4-oxo-4,5-dihydrothiazol-2-yl]amino]pentanedioic acid **391872-84-7P**, 5-[4-[4-[((2S)-2-Hydroxy-3-phenoxypropyl]amino)piperidin-1-yl]benzylidene]-2-morpholin-4-ylthiazol-4-one
RL: FFD (Food or feed use); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; prepn. of thiazolidinone derivs. as .beta.3 adrenergic receptor agonists, antidiabetics, and antiobesity agents)

RN 391872-50-7 CAPLUS
CN 2H-Benzimidazol-2-one, 1,3-dihydro-4-[(2S)-2-hydroxy-3-[[1-[4-[[2-(methylamino)-4-oxo-5(4H)-thiazolylidene]methyl]phenyl]-4-piperidinyl]amino]propoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 391872-51-8 CAPLUS
CN 2H-Benzimidazol-2-one, 1,3-dihydro-4-[(2S)-2-hydroxy-3-[[1-[4-[[2-[[2-(4-morpholinyl)ethyl]amino]-4-oxo-5(4H)-thiazolylidene]methyl]phenyl]-4-piperidinyl]amino]propoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

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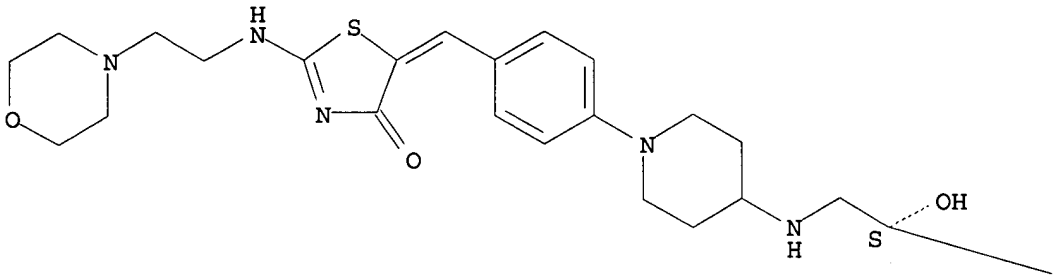

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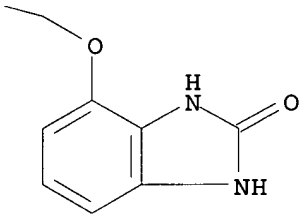

RN 391872-52-9 CAPLUS
CN 2H-Benzimidazol-2-one, 1,3-dihydro-4-[(2S)-2-hydroxy-3-[[1-[4-[[4-oxo-2-[[1-(phenylmethyl)-4-piperidinyl]amino]-5(4H)-thiazolylidene]methyl]phenyl]-4-piperidinyl]amino]propoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

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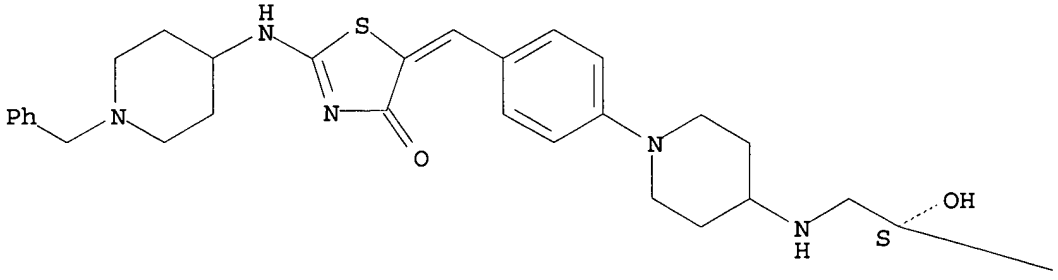
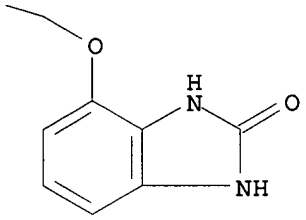
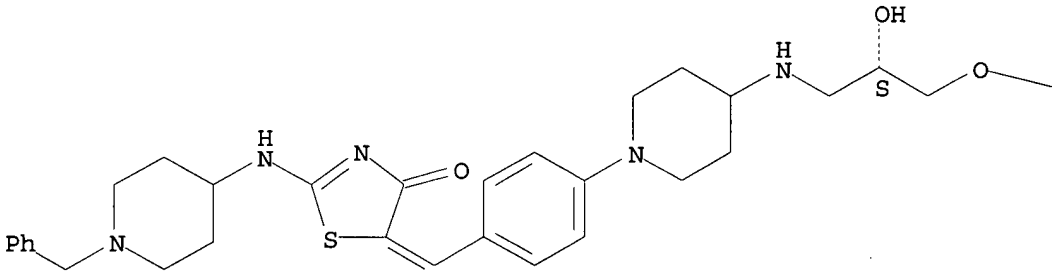
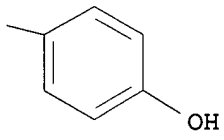




RN 391872-53-0 CAPLUS
CN 4(5H)-Thiazolone, 5-[[4-[4-[[(2S)-2-hydroxy-3-(4-hydroxyphenoxy)propyl]amino]-1-piperidinyl]phenyl]methylene]-2-[[1-(phenylmethyl)-4-piperidinyl]amino]- (9CI) (CA INDEX NAME)

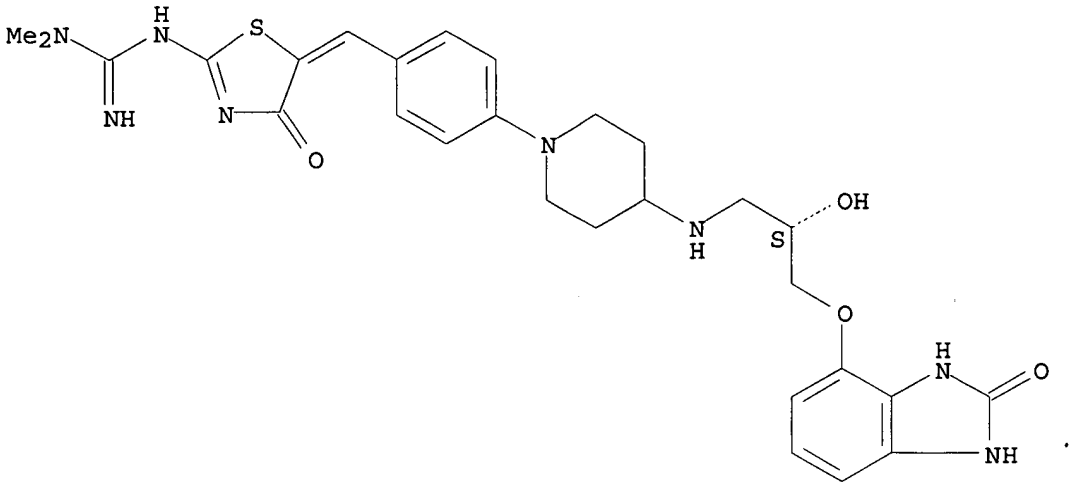
Absolute stereochemistry.
Double bond geometry unknown.





RN 391872-55-2 CAPLUS
CN Guanidine, N'-[5-[[4-[4-[[(2S)-3-[(2,3-dihydro-2-oxo-1H-benzimidazol-4-yl)oxy]-2-hydroxypropyl]amino]-1-piperidinyl]phenyl]methylene]-4,5-dihydro-4-oxo-2-thiazolyl]-N,N-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 391872-58-5 CAPLUS
CN .beta.-Alanine, N-[5-[[4-[4-[[(2S)-3-[(2,3-dihydro-2-oxo-1H-benzimidazol-4-yl)oxy]-2-hydroxypropyl]amino]-1-piperidinyl]phenyl]methylene]-4,5-dihydro-4-oxo-2-thiazolyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

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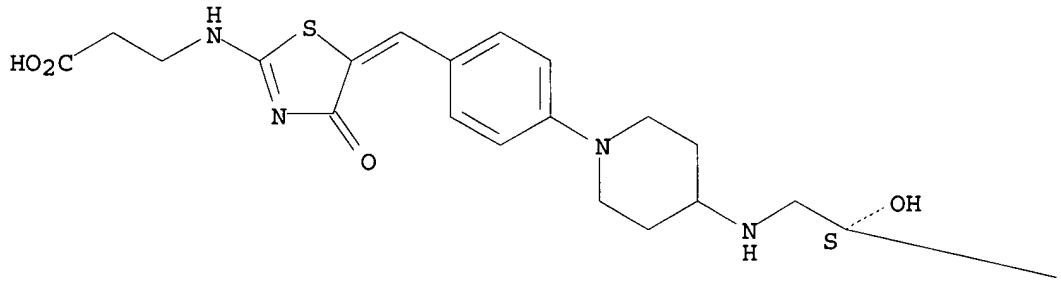

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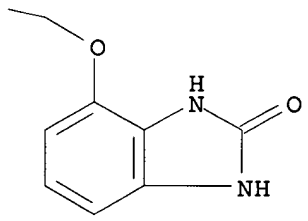
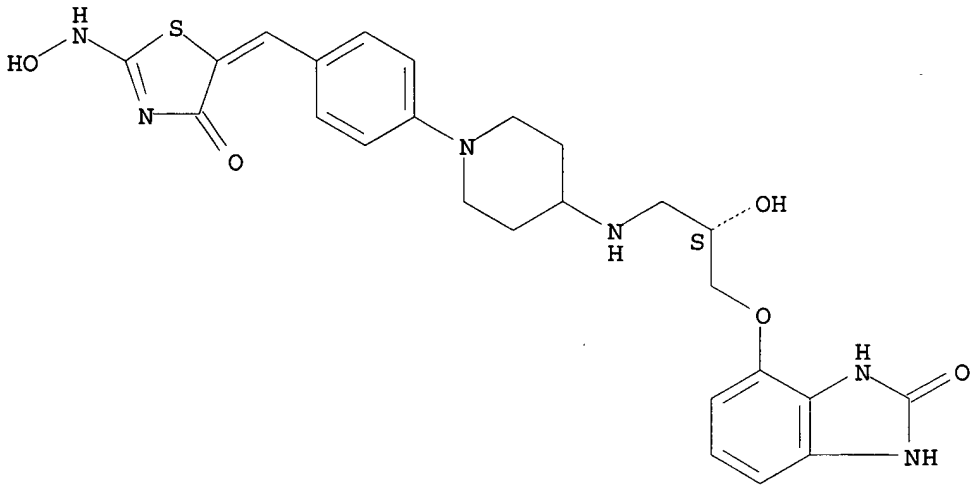


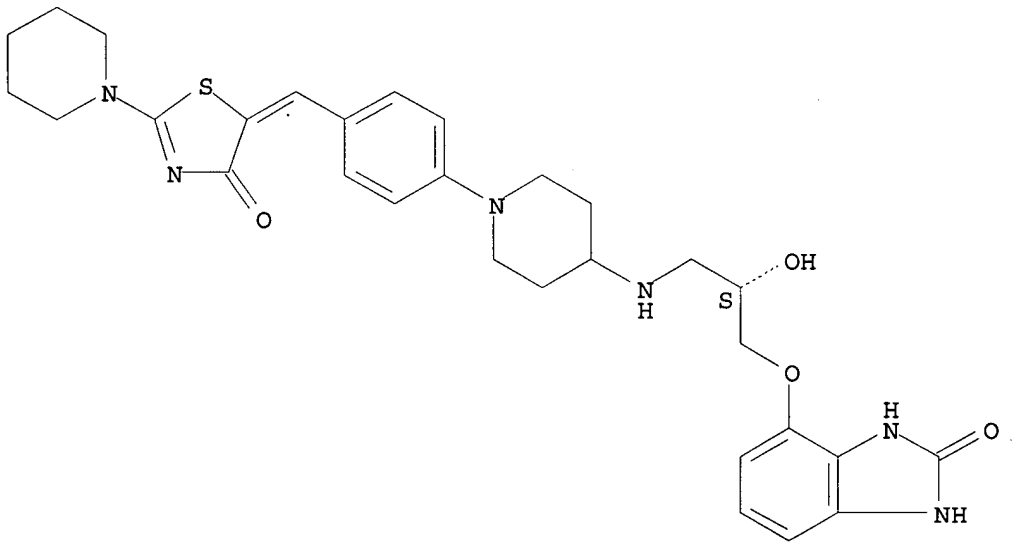
RN 391872-59-6 CAPLUS
CN 2,4-Thiazolidinedione, 5-[[4-[4-[[(2S)-3-[(2,3-dihydro-2-oxo-1H-benzimidazol-4-yl)oxy]-2-hydroxypropyl]amino]-1-piperidinyl]phenyl]methylene]-, 2-oxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



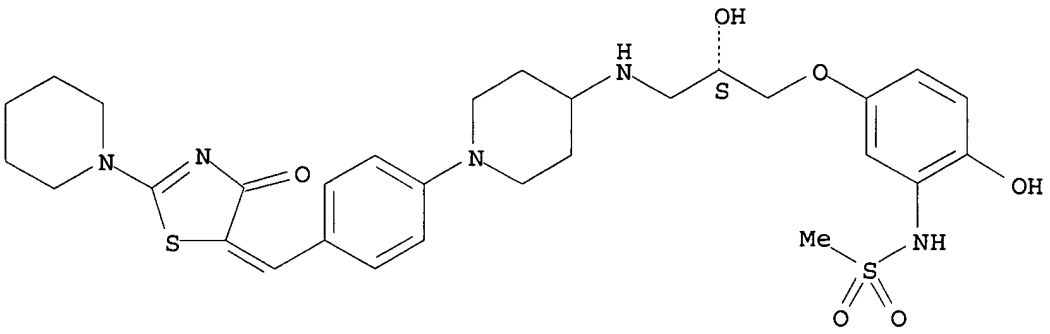
RN 391872-61-0 CAPLUS
CN 2H-Benzimidazol-2-one, 1,3-dihydro-4-[(2S)-2-hydroxy-3-[[1-[4-[[4-oxo-2-(1-piperidinyl)-5(4H)-thiazolylidene]methyl]phenyl]-4-piperidinyl]amino]propoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



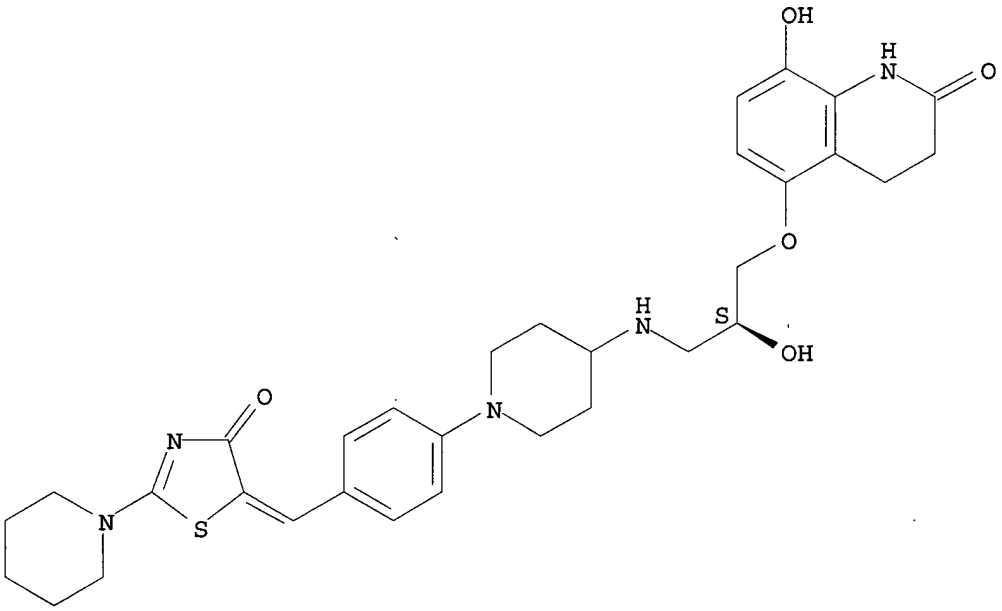
RN 391872-63-2 CAPLUS
CN Methanesulfonamide, N-[2-hydroxy-5-[(2S)-2-hydroxy-3-[[1-[4-[[4-oxo-2-(1-piperidinyl)-5(4H)-thiazolylidene]methyl]phenyl]-4-piperidinyl]amino]propoxy]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



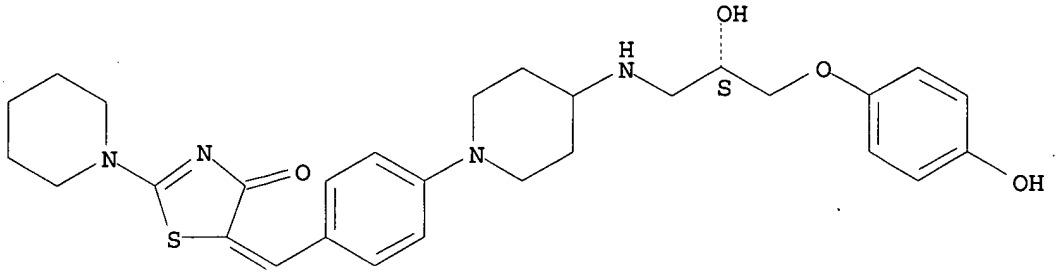
RN 391872-64-3 CAPLUS
CN 2(1H)-Quinolinone, 3,4-dihydro-8-hydroxy-5-[(2S)-2-hydroxy-3-[[1-[4-[[4-oxo-2-(1-piperidinyl)-5(4H)-thiazolylidene]methyl]phenyl]-4-piperidinyl]amino]propoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



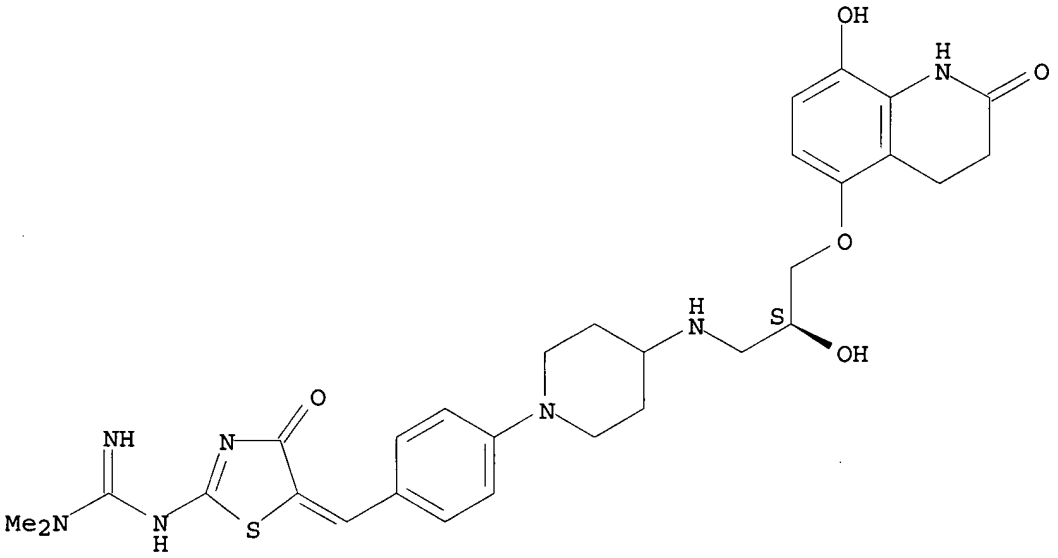
RN 391872-65-4 CAPLUS
CN 4(5H)-Thiazolone, 5-[[4-[4-[[(2S)-2-hydroxy-3-(4-hydroxyphenoxy)propyl]amino]-1-piperidinyl]phenyl]methylene]-2-(1-piperidinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



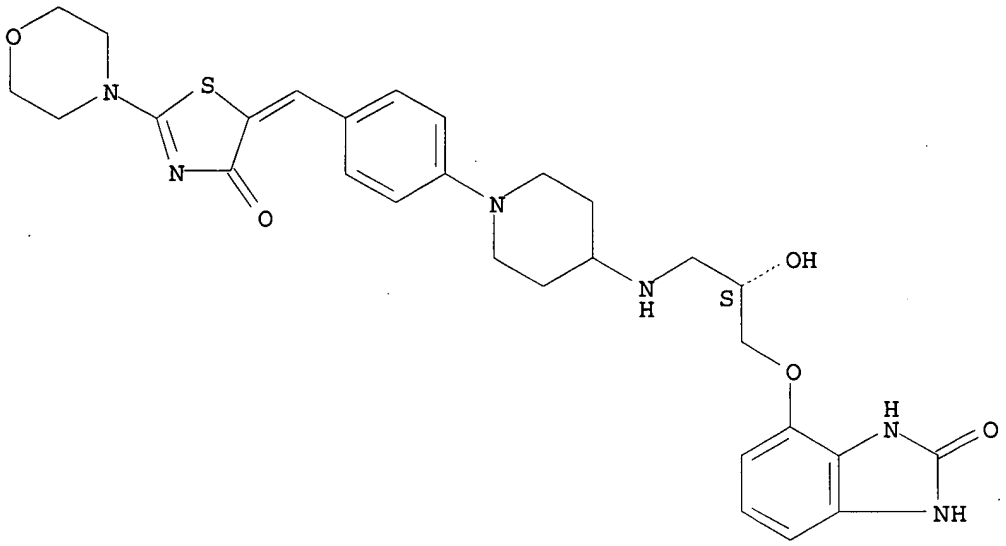
RN 391872-66-5 CAPLUS
CN Guanidine, N'-[4,5-dihydro-5-[[4-[4-[[(2S)-2-hydroxy-3-[(1,2,3,4-tetrahydro-8-hydroxy-2-oxo-5-quinolinyl)oxy]propyl]amino]-1-piperidinyl]phenyl]methylene]-4-oxo-2-thiazolyl]-N,N-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 391872-67-6 CAPLUS
CN 2H-Benzimidazol-2-one, 1,3-dihydro-4-[(2S)-2-hydroxy-3-[[1-[4-[[2-(4-morpholinyl)-4-oxo-5(4H)-thiazolylidene]methyl]phenyl]-4-piperidinyl]amino]propoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 391872-68-7 CAPLUS
CN 2H-Benzimidazol-2-one, 1,3-dihydro-4-[(2S)-2-hydroxy-3-[[1-[4-[[2-(4-methyl-1-piperazinyl)-4-oxo-5(4H)-thiazolylidene]methyl]phenyl]-4-piperidinyl]amino]propoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

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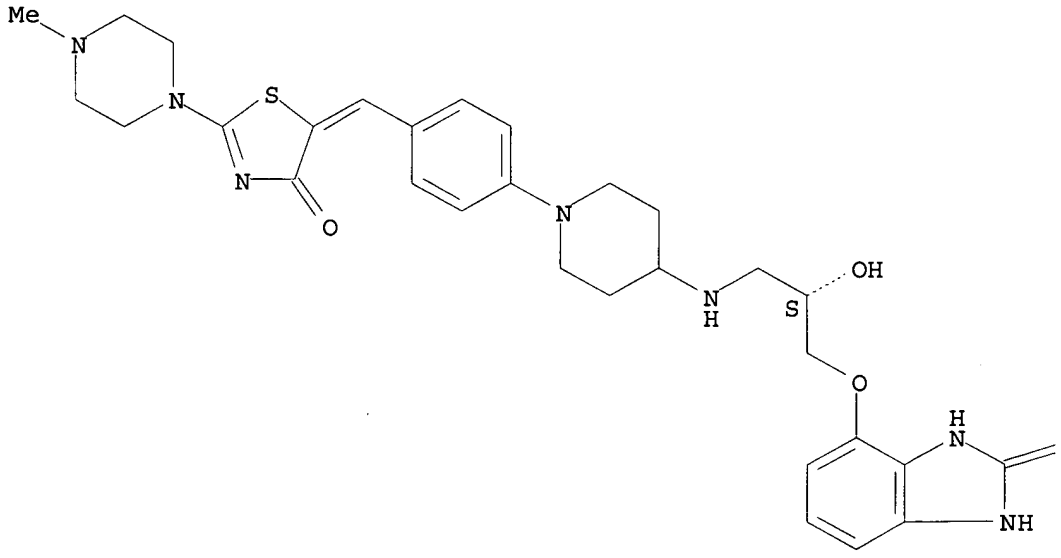
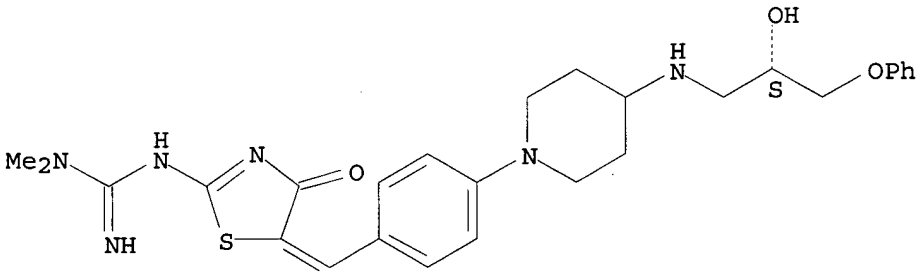


=O

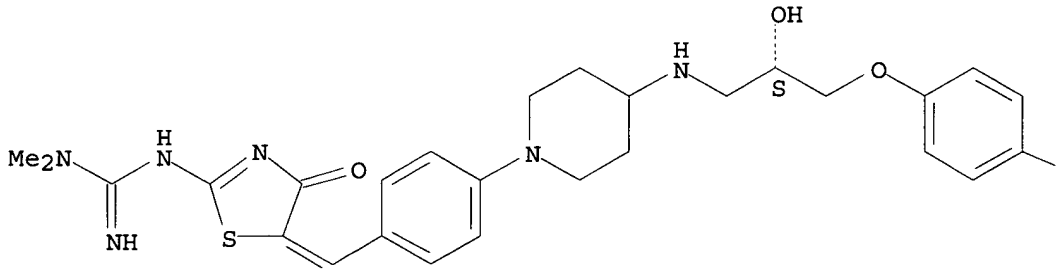
RN 391872-69-8 CAPLUS
CN Guanidine, N'-[4,5-dihydro-5-[[4-[4-[[(2S)-2-hydroxy-3-phenoxypropyl]amino]-1-piperidinyl]phenyl]methylene]-4-oxo-2-thiazolyl]-N,N-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 391872-70-1 CAPLUS
CN Guanidine, N'-[4,5-dihydro-5-[[4-[4-[[(2S)-2-hydroxy-3-(4-hydroxyphenoxy)propyl]amino]-1-piperidinyl]phenyl]methylene]-4-oxo-2-thiazolyl]-N,N-dimethyl- (9CI) (CA INDEX NAME)

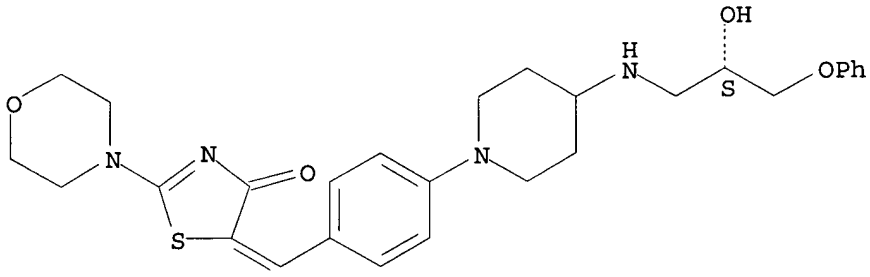
Absolute stereochemistry.
Double bond geometry unknown.



OH

RN 391872-71-2 CAPLUS
CN 4(5H)-Thiazolone, 5-[[4-[4-[[(2S)-2-hydroxy-3-phenoxypropyl]amino]-1-piperidinyl]phenyl]methylene]-2-(4-morpholinyl)-, dihydrochloride (9CI) (CA INDEX NAME)

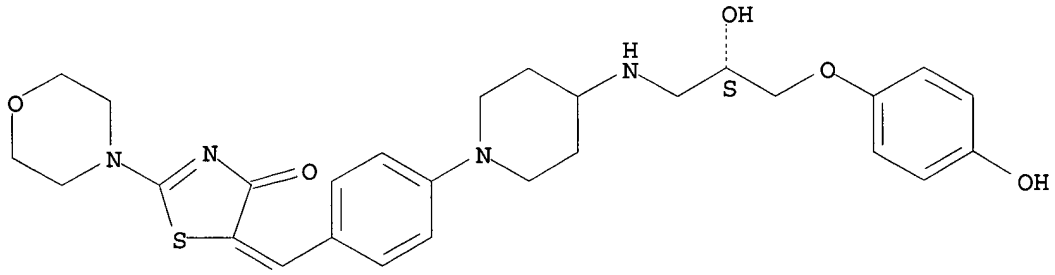
Absolute stereochemistry.
Double bond geometry unknown.



●2 HCl

RN 391872-72-3 CAPLUS
CN 4(5H)-Thiazolone, 5-[[4-[4-[[(2S)-2-hydroxy-3-(4-hydroxyphenoxy)propyl]amino]-1-piperidinyl]phenyl]methylene]-2-(4-morpholinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 391872-73-4 CAPLUS
CN 4(5H)-Thiazolone, 5-[[4-[4-[[(2S)-2-hydroxy-3-(4-hydroxyphenoxy)propyl]amino]-1-piperidinyl]phenyl]methylene]-2-(4-methyl-1-piperazinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

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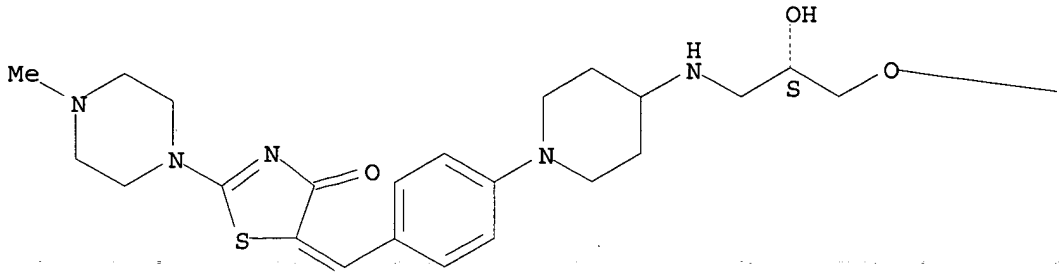

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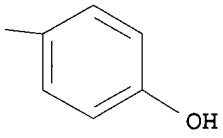
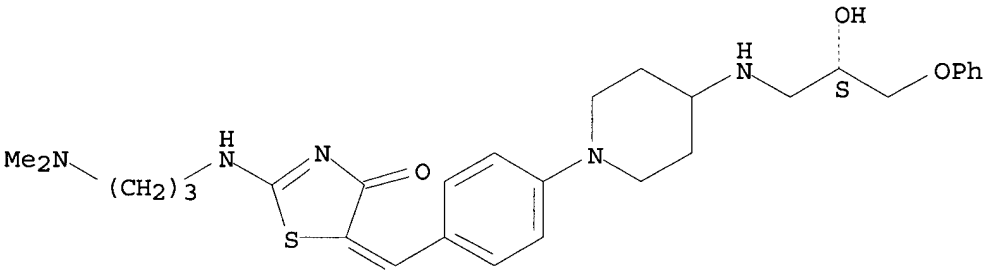


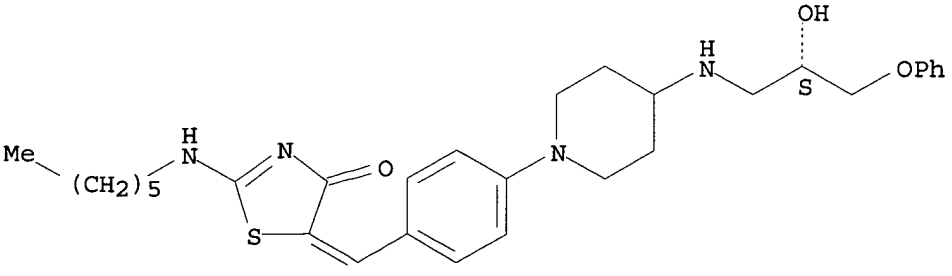
RN 391872-75-6 CAPLUS
CN 4(5H)-Thiazolone, 2-[[3-(dimethylamino)propyl]amino]-5-[[4-[4-[[(2S)-2-hydroxy-3-phenoxypropyl]amino]-1-piperidinyl]phenyl]methylene]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 391872-76-7 CAPLUS
CN 4(5H)-Thiazolone, 2-(hexylamino)-5-[[4-[4-[[(2S)-2-hydroxy-3-phenoxypropyl]amino]-1-piperidinyl]phenyl]methylene]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 391872-78-9 CAPLUS
CN L-Glutamic acid, N-[5-[[4-[4-[[(2S)-3-[(2,3-dihydro-2-oxo-1H-benzimidazol-4-yl)oxy]-2-hydroxypropyl]amino]-1-piperidinyl]phenyl]methylene]-4,5-dihydro-4-oxo-2-thiazolyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

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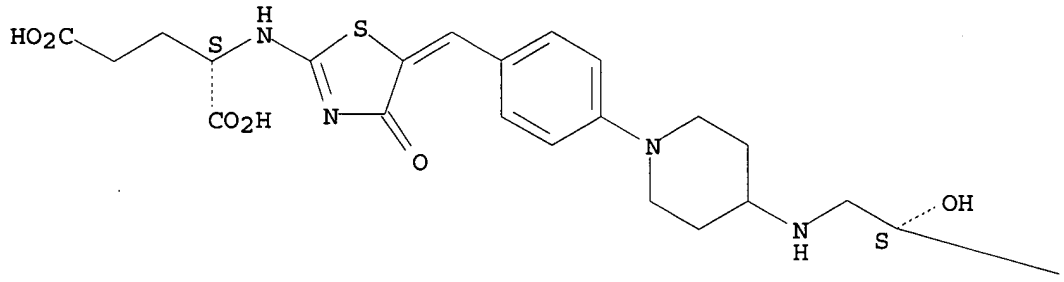

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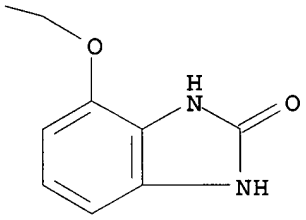
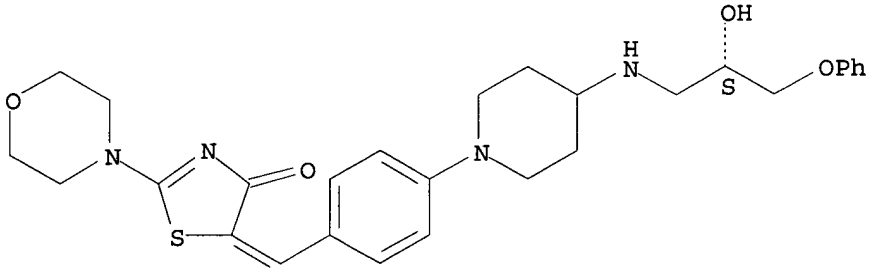


RN 391872-84-7 CAPLUS
CN 4(5H)-Thiazolone, 5-[[4-[4-[[(2S)-2-hydroxy-3-phenoxypropyl]amino]-1-piperidinyl]phenyl]methylene]-2-(4-morpholinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AN 2002:72070 CAPLUS
DN 136:134677
TI Substituted 2-(S)-hydroxy-3-[(piperidin-4-yl-methyl)amino]propyl ethers and substituted 2-aryl-2-(R)-hydroxy-1-(piperidin-4-yl-methyl)ethylamines as beta-3 adrenergic receptor agonists, antidiabetics, and antiobesity agents
IN Steffan, Robert John; Ashwell, Mark Anthony; Pelletier, Jeffrey Claude; Solvibile, William Ronald; Matelan, Edward Martin
PA American Home Products Corporation, USA
SO PCT Int. Appl., 216 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002006255	A2	20020124	WO 2001-US22363	20010716
	WO 2002006255	A3	20020321		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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	US 2002037907	A1	20020328	US 2001-903738	20010712
	US 6506901	B2	20030114		
PRAI	US 2000-218753P	P	20000717		

OS MARPAT 136:134677
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention provides title compds. I and their pharmaceutically acceptable salts [wherein A = OCH2, bond; R = (un)substituted aryl or certain N/O/S heterocyclyl; R1 = (cyclo)alkyl, alkoxy, (cyclo)alkylamino, (un)substituted aryl, arylamino, arylalkyl, or heterocyclyl; Z = bond, SO2, CO]. I are useful in treating or inhibiting metabolic disorders related to insulin resistance or hyperglycemia (typically assocd. with obesity or glucose intolerance), atherosclerosis, gastrointestinal disorders, neurogenic inflammation, glaucoma, ocular hypertension, and frequent urination. The compds. are particularly useful in the treatment or inhibition of type II diabetes. They are also useful for increasing lean meat deposition and/or increasing the lean meat to fat ratio in animals, particularly mammals. Approx. 240 individual compds. and addnl. salts were prepd. by either std. or combinatorial methods. For instance, invention compd. II was prepd. by reaction of the (S)-isomeric epoxide III with the corresponding amine. II had an EC50 of 0.001 .mu.M against cloned human .beta.3 adrenoceptors in vitro, with a maximal response comparable to isoproterenol.

IT **392688-96-9P**, 1-[4-[4-[[[(2S)-2-Hydroxy-3-[(8-hydroxy-2-oxo-1,2,3,4-tetrahydroquinolin-5-yl)oxy]propyl]amino]methyl]piperidine-1-sulfonyl]phenyl]-3-octylurea
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; prepn. of piperidine hydroxyaminopropyl ether and

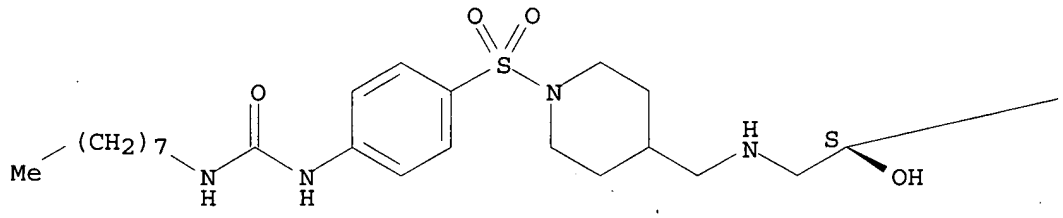
hydroxyethylamine derivs. as .beta.3 adrenergic receptor agonists, antidiabetics, and antiobesity agents)

RN 392688-96-9 CAPLUS

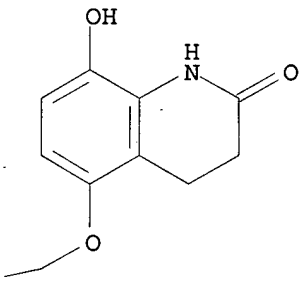
CN 4-Piperidinemethanamine, N-[(2S)-2-hydroxy-3-[(1,2,3,4-tetrahydro-8-hydroxy-2-oxo-5-quinolinyl)oxy]propyl]-1-[[4-[[(octylamino)carbonyl]amino]phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



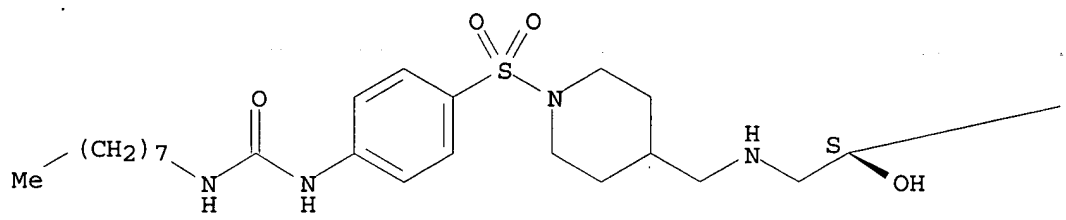
IT **392692-41-0P**, 1-[4-[4-[[[(2S)-2-Hydroxy-3-[(8-benzyloxy-2-oxo-1,2,3,4-tetrahydroquinolin-5-yl)oxy]propyl]amino]methyl]piperidine-1-sulfonyl]phenyl]-3-octylurea
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of piperidine hydroxyaminopropyl ether and hydroxyethylamine derivs. as .beta.3 adrenergic receptor agonists, antidiabetics, and antiobesity agents)

RN 392692-41-0 CAPLUS

CN 4-Piperidinemethanamine, N-[(2S)-2-hydroxy-3-[[1,2,3,4-tetrahydro-2-oxo-8-(phenylmethoxy)-5-quinolinyl]oxy]propyl]-1-[[4-[[(octylamino)carbonyl]amino]phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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